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SCIENCE UNDER SIEGE: SCIENTIFIC INTEGRITY AT THE ENVIRONMENTAL PROTECTION AGENCY

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

ONE HUNDRED TENTH CONGRESS

SECOND SESSION

SEPTEMBER 18, 2008

Serial No. 110–149

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SCIENCE UNDER SIEGE: SCIENTIFIC INTEGRITY AT THE ENVIRONMENTAL PROTECTION AGENCY

THURSDAY, SEPTEMBER 18, 2008

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, D.C.

The subcommittee met, pursuant to call, at 10:08 a.m., in room 2322 of the Rayburn House Office Building, Hon. Bart Stupak (chairman) presiding.

Members present: Representatives Stupak, Melancon, Green, Inslee, Dingell (ex officio), Shimkus, Walden, Burgess, and Barton (ex officio).

Staff present: Scott Schloegel, John Sopko, John Arlington, Paul Jung, Kyle Chapman, Katherine Graham, Alan Slobodin, Karen Christian, and Whitney Drew.

OPENING STATEMENT OF HON. BART STUPAK, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. STUPAK. This meeting will come to order.

Today we have a hearing entitled "Science under Siege: Scientific Integrity at the Environmental Protection Agency." Each member will have 5 minutes for an opening statement. I will begin.

The mission of the U.S. Environmental Protection Agency, EPA, is to protect human health and the environment. This mission is best accomplished by regulatory decisions based on reliable science. However, indications are that the Environmental Protection Agency may instead be using selective science in regulatory decisions.

The purpose of our hearing is to review the apparent lack of scientific integrity in parts of the EPA. We will examine four specific examples. One, a report from the Union of Concerned Scientists that found significant political interference in scientific work at EPA; two, the supposed "streamlining" of the Integrated Risk Information System, IRIS, which actually makes it more difficult for EPA to publish scientific analyses on chemical risk; third, the removal of Dr. Deborah Rice from a scientific peer review panel at the request of the chemical industry; and fourth, the EPA's adoption of a since-discredited clean-up plan for the chemical toxaphene at the Hercules Superfund near Brunswick, Georgia.

The Union of Concerned Scientists, UCS, conducted a study on political interference at the EPA. Scientists reported that they personally experienced political interference in the last 5 years and being directed to inappropriately exclude or alter technical information from EPA scientific documents. Scientists often identified the White House Office of Management and Budget as the primary source of external interference. The Union of Concerned Scientists' study paints a picture far from the open scientific debate that we should expect from a science-based regulatory agency.

The Integrated Risk Information System, or IRIS, is the U.S. government's catalog of the health effects of toxic chemicals. To have information placed into IRIS, EPA scientists carefully evaluate the science of each chemical and provide relevant data in the system. On April 10, 2008, the EPA instituted a new streamlined process for IRIS, which actually increases the number of steps in the evaluation process. Notably, the new process now requires approval by OMB at least twice prior to final posting in IRIS. As expected, this new process will delay the reporting of chemical hazards and make it more difficult for EPA scientists to publish their data in IRIS.

Dr. Deborah Rice was invited by EPA to chair a 5-member peer review panel to update the IRIS assessment of the chemical deca, a flame retardant used on plastics and textiles. After the deca peer review panel concluded their business and posted their final comments, the EPA removed Dr. Rice from the panel and erased her comments from the report at the behest of the American Chemistry Council. Their reasons included the fact that Dr. Rice provided testimony to the Maine Legislature in her capacity as the Maine state toxicologist on their proposal to ban deca. Dr. Rice was informed of this decision by telephone. She received no written explanation. It appears that Dr. Rice was removed from the peer review panel because she had expertise on the chemical in question and was asked to provide that expertise to a state legislature.

Toxaphene is an insecticide that was widely used in the United States on crops, fish, and livestock before it was completely banned in 1990 due to health hazards. Brunswick, Georgia, is the home of the Hercules 009 landfill, a superfund site where toxaphene waste was dumped from 1975 to 1980. This superfund site abuts the local elementary school and the community is concerned that toxaphene and its harmful breakdown products may persist at that site. Since the Hercules 009 became a superfund site in 1984, EPA continues to use an outdated, inaccurate scientific method to detect the toxaphene, while other federal agencies, including the Agency for Toxic Substances and Disease Registry, ATSDR, the Army Corps of Engineers, and EPA's Inspector General recommended the use of the negative ion mass spectroscopy, NIMS, as they call it. EPA has not adopted NIMS as their standard test. In addition, the EPA's method to clean up the Hercules 009 site is based on an article published in the journal Regulatory Toxicology and Pharmacology, which has been assailed by scientists as having an industry bias. In addition, it appears the Hercules Corporation has hired the Weinberg Group, a consulting firm under investigation by our committee, to determine the toxicity of toxaphene. These actions paint a suspicious picture of questionable regulatory decisionmaking.

Today we will hear from several witnesses. Our first panel will include Dr. Francesca Grifo of the Union of Concerned Scientists, who will discuss her organization's report, and Mr. John Stephenson of the Government Accountability Office, who will discuss GAO's report on the new IRIS changes.

Our second panel will include Dr. Rice, who will testify about her removal from the EPA peer review panel, Dr. Jennifer Sass from the National Resources Defense Council, who will tell us how the new IRIS changes will affect environmental science, Mr. Daniel Parshley of the Glynn Environmental Coalition to discuss issues at the Hercules superfund site, and Sharon Kneiss of the American Chemistry Council, who will testify about ACC's role in the removal of Dr. Rice from the EPA's peer review panel.

Finally, we will hear from Marcus Peacock, Deputy Director, and George Gray, Ph.D., Assistant Administrator for Research and Development at the Environmental Protection Agency.

I look forward to the testimony of all the witnesses. I believe today's testimony will show how the EPA has dangerously undermined the role of science in regulatory decision making. The EPA under the Bush Administration appears to have put politics before science, to the harm of not just the environment but to the fundamentals of science. Science is not a Republican or Democratic issue. It must be based on facts and not political affiliation. I sincerely hope today's testimony will be taken seriously by the EPA and that they will work seriously to ensure the science will return to its proper role within the Agency.

That concludes my opening statement.

Mr. STUPAK. I will turn to my friend, Mr. Shimkus from Illinois, for your opening statement, sir.

OPENING STATEMENT OF HON. JOHN SHIMKUS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

Mr. SHIMKUS. Thank you, Mr. Chairman, for convening this oversight hearing.

Over the last year, some individuals and advocacy groups including some of the witnesses before us today have charged that the EPA has interfered with certain scientific decisions for political reasons or at the behest of industry. Dr. Francesca Grifo of the Union of Concerned Scientists will testify on the first panel as she has testified before the House and Senate panels about her organization's report, Interference at the EPA. After reviewing the testimony in that, I guess part of the irony of this is that the Union of Concerned Scientists not using a scientific poll in this Interference at the EPA, which we all know about polling and we know the scientific process and we know one that is not.

A number of hearings have been held in the House and Senate discussing alleging interference, in particular this year's hearing on the National Ambient Air Quality Standards, or NAAQS. This committee and this subcommittee have a long history of examining EPA on issues of scientific decisionmaking. These issues are altogether appropriate topics for an oversight hearing. What troubles me is the way this hearing has come together and the title of the hearing implies that the Majority has drawn a conclusion before we have even obtained testimony and all the evidence. It is important in any investigation to take the time to gather the facts, to hear both sides of the story and to weight and vet the information you receive. Given the amount of attention that has been devoted to alleged political interference at the EPA over the last year, it may be tempting to make assumptions and prematurely draw conclusions. We are presented today with three separate cases that the Majority contends are examples of science under siege, but based upon the incomplete factual record of today, I cannot conclude one way or the other that EPA made the decisions it did because of political or industry influence or that anything was done wrong. We all know there are good-faith disputes over science and disagreements with policy calls that happen every day at the EPA. In fact, the background on each of these cases is complex and the three case studies may not even be particularly strong examples in support of the charge of political interference.

For instance, let us consider the case of the cleanup plan for the Hercules site in Georgia. EPA implemented a plan to clean up toxaphene, a pesticide, at a landfill site. A dispute arose as to whether the EPA had picked the right method to test for toxaphene in the soil and the groundwater. Two EPA Office of Inspector General reports issued in 2005 essentially concluded that EPA would not be able to determine whether its cleanup plan was effective because its testing method was incapable of measuring whether degraded toxaphene was present. In responding to these reports, EPA cited an article published in the Regulatory Toxicology and Pharmacology Journal as a basis for its Hercules toxicity calculations. Now, some in the scientific community believe this journal's efforts to identify conflicts of interest among its board when selecting articles for publication are inadequate and therefore the Agency's reliance on this article was improper. It may be that this article does not support the cleanup plan EPA adopted or does not represent the best science on toxaphene. It may also be that the Agency's delay in resolving the questions surrounding the testing for toxaphene is indefensible. But this does not mean that the EPA's decision was improperly influenced by industry and we have yet to uncover any evidence to substantiate that claim. Indeed, the Committee has not even interviewed the EPA staff who worked on the cleanup plan or collected a single document on the issue. Let me just highlight that. The Committee has not interviewed the EPA staff who worked on the cleanup plan or collected a single document on this issue.

I have similar questions about the EPA's actions with respect to peer review panel for deca, a flame retardant. Dr. Deborah Rice was the chair of the panel but her comments were removed from the peer review report due to possible appearance of impartiality after the American Chemistry Council informed EPA that Dr. Rice has testified before the Maine Legislature about deca. Dr. Rice and the ACC are witnesses on the second panel, and Dr. George Gray of EPA, who ultimately removed Dr. Rice's comments, is on our third panel. At least with respect to this case, we may be able to hear all sides of the story because the parties are here. The removal of Dr. Rice's comments is obviously a very sensitive issue because it involves not only the integrity of the peer review process but also Dr. Rice's professional reputation. So we must be especially careful when we try to sort through the facts in order to understand the EPA's rules on impartiality and peer review panels and how they are applied in this case. Does the fact that Dr. Rice believed that the evidence supported banning deca and that reasonable alternatives exist to deca mean that she is impartial when it comes to developing a toxicological assessment of the chemical? Is a determination about banning deca or that alternatives exist a separate issue from the types of issues Dr. Rice reviewed as a member of the deca panel? Does expressing any opinion on toxicity of a chemical prevent you from serving on a peer review panel on IRIS matters? These matters are not black and white and I think it is fair to say that reasonable minds can disagree about when a person's opinions or professional experience might cause them to be impartial on a certain issue. I hope the witnesses today will give us some guidance on this issue and their thoughts on whether the EPA process are sufficient or whether they can be improved.

Finally, Mr. John Stephenson of GAO is here to discuss his office report on the recent changes to EPA's Integrated Risk Information System, or IRIS. EPA made a number of changes to the process to allow for participation by other government agencies, the Office of Management and Budget, and the public. The GAO report contends that these changes have slowed the IRIS review process almost to a halt. I am interested in learning why EPA made the changes it did and whether the process can be improved so IRIS risk assessments are completed in a timely manner, but again, I think we should not rush to conclude that simply because changes were made that they were made by this Administration that they are not valid reasons for interagency involvement in the IRIS process, and that is my point. It is one thing to conclude that EPA has been slow to adopt the prevailing science and has made the wrong policy decisions. It is an entirely different matter to attribute that mistake to political or industry interference. That is a serious charge, and if it is happening, EPA must be held accountable, but we need to do our work and make sure that the facts support the charge.

Thank you, Mr. Chairman. I yield back the balance of my time.

Mr. STUPAK. Thank you, Mr. Shimkus.

Mr. Dingell for an opening statement, please.

OPENING STATEMENT OF HON. JOHN D. DINGELL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. DINGELL. Mr. Chairman, thank you.

First of all, this is an important hearing, and second of all, I thank you and commend you for holding it.

Scientific integrity is an essential ingredient of every decision that is made by the Environmental Protection Agency. Unfortunately, there is a substantial question as to whether or not that is always the case. I would note that this has been a continuing problem to me and to this committee for years, and it appears to be continuing under the current Administration. So the question here is, is this the case under the current Administration and why is there a problem under this Administration?

There is growing evidence that the Congress, the States, the local governments, the public, and even other countries cannot rely on EPA for honest science. I repeat, I have found that to be the situation which has confronted this committee for a number of years.

The landmark survey of EPA scientists conducted by the Union of Concerned Scientists, UCS, confirms what many had feared, that the Bush Administration's political interference now going on with EPA scientists is both pervasive and frequent.

The UCS scientist survey found that more than 500 EPA scientists knew of many or some cases where EPA political appointees had interfered with scientific decisions.

Nearly 100 EPA scientists identified the White House Office of Management and Budget as the primary source of external interference and more than 500 scientists said they feared retaliation for speaking candidly about EPA's scientific work. Clearly then, there is reason to believe we are not talking about an isolated instance.

The testimony we will hear today exposes a broad pattern of political meddling by the Bush Administration directed at EPA scientists and its science.

The prime example of the Administration's recent changes to the Integrated Risk Information System, IRIS process, under which chemicals are evaluated to determine the extent to which they may be hazardous to the public health, is a matter of concern to the committee. For 20 years, government agencies both here and abroad have relied on IRIS for scientific, reliable information on the human health effects of hundreds of widely used chemicals. Drinking water standards and workplace exposure standards are based on scientific data contained in the IRIS database.

Undeterred by the success of the IRIS system, however, the Bush Administration has changed the IRIS process to all but halt the addition of new chemicals to the database. What was once a careful and thoughtful scientific process managed by EPA scientists has become a cumbersome, bureaucratic, political exercise run by OMB, and the studies and the analysis that you have on this matter, Mr. Chairman, will tend to buttress the complexity that is now built into this system.

Under the new system, the two largest polluters in the United States—the Department of Defense and the Department of Energy—are permitted to provide secret comments to OMB, which then has the final say on what goes into the IRIS system. We must inquire why these two agencies should be permitted to submit secret comments to OMB and why it is that even EPA is not permitted to see these comments. It raises questions as to the worth of the system under this kind of curious modification. And because all of this is now done in secrecy, it is entirely unclear as to who has or does not have a hand in the process. In short, what was once a process marked by transparency, candor, and credibility is now apparently marked by secrecy, manipulation, influence, and probably connivers.

Mr. Chairman, I particularly want to welcome to this hearing Dr. Deborah Rice, chief toxicologist for the State of Maine. Dr. Rice's removal from the IRIS peer review panel at the request of the chemical industry is curious, and it is to be assumed that this is because she testified before the Maine Legislature. Clearly, this is disgraceful. I look forward to hearing from EPA management about specific steps they are taking to rectify these problems and to protect the scientific integrity of the Agency and at the Agency. I also will look forward to hearing from the Administration what they propose to do to see to it that the taint of possible political manipulation or influence at the IRIS process is corrected in a proper fashion.

Mr. Chairman, I thank you.

Mr. STUPAK. I thank the chairman.

Mr. Barton for an opening statement, please.

OPENING STATEMENT OF HON. JOE BARTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BARTON. Thank you, Chairman Stupak. Thank you for convening this hearing concerning the Environmental Protection Agency.

Republicans on the Committee welcome oversight of the Environmental Protection Agency. The topics discussed in this hearing, the EPA's Integrated Risk Information System, the composition of EPA peer review panels, and the management of Superfund sites are all important issues and important to public health. The title of this hearing, however, does trouble me. It in itself could be considered to be an attack on the EPA, or if you want to say, a surrogate attack on the Bush Administration. The title of this hearing makes a serious charge that science at the EPA is under siege and that its integrity may have been compromised. Has this really happened? Have scientific conclusions been improperly influenced by politics or by interested parties? These are certainly critical questions but somehow I don't believe that we are going to get too many facts at this hearing to really answer those questions.

The Majority offers three case studies today to make the argument that the EPA and its scientific conclusions have somehow been improperly influenced. One case involves changes to the IRIS system, which were the subject of a GAO report issued last spring. The second involves a Hercules Superfund cleanup site in Georgia, which has been the subject of some dispute due to the cleanup methods that the EPA adopted for the site. The third is a peer review of a chemical used in flame retardants known as deca that took place in early 2007 for the purpose of including certain information on the aforementioned IRIS system. Reviewer's comments were struck from the peer review report after concerns were raised about a potential conflict of interest. Both Dr. Deborah Rice, the reviewer, and the American Chemistry Council, the group that raised the concern to EPA, will testify today and I think that is a good thing. We will also hear from two organizations, the Union of Concerned Scientists and the Natural Resources Defense Council, about their experiences with the EPA decision making.

I am not prepared today to conclude one way or the other whether the Agency was right or wrong or whether they influenced data. In the Hercules case, for example, the Committee has not even talked to the EPA project managers who oversaw the cleanup to get a sense of why they adopted the cleanup method that they did or why they didn't use certain technologies to detect chemicals at the site. As far as I know, no documents have been requested from the EPA or, for that matter, anyone else. I understand that the Majority may suggest that EPA improperly relied on a particular journal article because a journal has an affiliation with industry.

The Agency's reliance on the article and its role in determining the Hercules cleanup is a legitimate scientific issue. But at least in my opinion, without talking to the people involved and obtaining the documents, it is somewhat of a leap to judge the EPA's motives. Shooting first and asking questions later does get results, especially if you hit your target, but better science probably won't be one of them.

The bottom line is, Mr. Chairman, that whether we are a Republican or a Democrat, we all want the EPA to develop and use the best science possible, and I emphasize the best science possible, when making regulatory decisions. An agency like EPA that is entrusted with the public health cannot be allowed to ignore honest scientific reports. It must be required to apply the data objectively but science is progressing and science does change. Good faith disputes about what the data is are just that, good-faith disputes. What we conclude from those data points, we can all have a different opinion, especially experts. It happens all the time. We should be very careful before we assign motives to those disputes and attribute differences in opinion to political meddling or industry influence. It is our job to keep an eye on both the politics and the science as members of this oversight subcommittee but it is not our job sometimes simply just to shoot at specific targets for political purposes.

We are having a hearing today, and again, I am not opposed to having this hearing, but I do think that we should have scheduled this particular hearing 2 years ago when the new Majority took over. I think it is a legitimate question for a different political majority to want to have an honest review of a different politically affiliated Administration's opinions and perhaps even system review processes about issues of this type. I don't really have a problem with that. But we are having this almost the last week that we are scheduled to be in regular session and it is just simply not the time to find the kind of facts and to develop the kind of database that we really need to develop if we are going to make some conclusions about the EPA, as the title of the hearing puts it, being under siege.

Our oversight and investigation responsibility, and I mean this, this subcommittee and the full committee under the chairmanship of John Dingell in the past and Mr. Bliley, Mr. Tauzin and myself in the recent past and now in the current sense with you, Mr. Stupak and Mr. Dingell as the full committee chairman is probably, and I shouldn't even say "probably," I will say it is the most effective oversight operation in the House of Representatives, so we should use it in an objective fashion to get the facts and then come to the conclusions.

Mr. Chairman, sometimes the risk of overlooking a problem is outweighed by the risk of underinvestigating one, and I really hope now that we have started this, and I mean this, let us really get all the facts. We all need an EPA that is objective. We all need an EPA that does use the best science and we all need an EPA that does provide the Congress and the country with the optimal solutions to our environmental problems. So again, I have no problem with this hearing. I do have a little bit of a problem with the timing of it and I hope that as we progress in this particular inquiry, that we do get the facts before we come up with conclusions.

With that, Mr. Chairman, I certainly respectfully yield back my time.

Mr. STUPAK. Well, thanks, Mr. Barton, and specifically as to the Hercules cleanup, you raised a couple of questions there and I just wanted to let you know that the committee staff on both sides have done due diligence here. We did invite the head of the Superfund program to testify but they said they couldn't make it. We specifically asked for a briefing on Hercules prior to the hearing. We are still waiting for the briefing. We also invited the EPA to send a witness from Region 4 who would be familiar with the site but again, we are still waiting for an answer from the EPA whether or not these people can testify. And you are right, we are running out of time so I guess bob-and-weave can only go so long, so we had to have our hearing. So some of those concerns are valid but I want you to know, we did ask for those witnesses because we do always try to have a full, complete hearing. Once in a while we just have to move forward if an agency is not going to cooperate with you and we didn't think a subpoena was necessary at this point in time. Maybe it will be in the future on this issue.

Mr. Burgess, opening statement, please.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. Thank you, Mr. Chairman, and I appreciate the recognition. I am going to submit my opening statement for the record because this is an important hearing and I do want that recorded but I do want to go off topic for just a moment and talk about something else because we are up against the end of a session and our time is limited.

This committee, this subcommittee in particular, has taken a leadership role with issues relating to individual privacy. We have focused on privacy-invading practices such as pretexting, spyware, and hacking. We recognize correctly the pernicious effects of information theft, identify theft, and theft of information in a free society, but this morning we are faced with stories on the news wires involving a governor of a State, a vice presidential nominee, and these assaults on the privacy of Governor Palin should be aggressively investigated and the perpetrators prosecuted to the fullest extent of federal law. This subcommittee has jurisdiction over this issue and should take the lead in this investigation.

The fact that Governor Palin's e-mail account was hacked and not only was it hacked but the information was then freely distributed on the World Wide Web and the information posted revealed only information of a personal nature because it was a personal e-mail account. As the Subcommittee on Oversight and Investigations, let us look to whether appropriate safeguards are in place by e-mail carriers such as Yahoo, MSN and Google against the malicious actions of those who would act to violate the personal privacy of a public individual. Theft of personal information is an asymmetric threat which can affect any one of us in public service and certainly any one of the constituents that we serve. We are obligated to maintain oversight of the telecommunications industry and ensure that no personal information is made inappropriately available. And if and when transgressions are uncovered, they need to be fully investigated and prosecuted under existing statutes.

Mr. Chairman, I thank you for the indulgence and I will yield back the balance of my time.

Mr. STUPAK. I thank the gentleman for his comments.

Mr. Melancon, opening statement?

Mr. MELANCON. No, I am going to waive.

Mr. STUPAK. OK. That concludes the opening statements by members and I am going to ask the witnesses to come forward. They are already seated, Mr. Stephenson and Dr. Grifo. It is the policy of this subcommittee to take all testimony under oath. Please be advised that you have the right under the rules of the House to be advised by counsel during your testimony. Do you wish to be represented by counsel?

Mr. STEPHENSON. No.

Mr. STUPAK. Dr. Grifo?

Ms. GRIFO. No.

Mr. STUPAK. I am going to ask if you would please rise and raise your right hand to take the oath.

[Witnesses sworn.]

Mr. STUPAK. Let the record reflect that the witnesses replied in the affirmative. Each of you are now under oath and you can give your opening statement. We would ask that you please try to limit it to 5 minutes, and your full statement will be made part of the record, so Mr. Stephenson, if you would like to start, please.

STATEMENT OF JOHN B. STEPHENSON, DIRECTOR, NATURAL RESOURCES AND ENVIRONMENT, U.S. GOVERNMENT ACCOUNTABILITY OFFICE

Mr. STEPHENSON. Thank you, Mr. Chairman and members of the subcommittee. I am here today to discuss our recent work on EPA's Integrated Risk Information System, or IRIS. It is a database that contains EPA's scientific position on the health effects and exposure of more than 540 toxic chemicals. IRIS is a critical component of EPA's capacity to support scientifically sound environmental decisions, policies, and regulations and is a cornerstone of scientific integrity at the Agency. My testimony today is based primarily on our March 2008 report and additional work we did to support a May 2008 testimony before the Senate.

Our work clearly shows that the IRIS database is at serious risk of becoming obsolete because EPA has not been able to complete timely, credible, scientific assessments or decrease its backlog of 70 ongoing assessments. Efforts to improve IRIS since 2000 have been thwarted by a combination of factors, including OMB and interagency reviews, EPA decisions to delay assessments to wait for new research or additional uncertainty analysis, and the compounding effects of continuous delays. Moreover, two new OMB interagency reviews involve other federal agencies in a manner that limits the credibility of these scientific assessments and hinders EPA's ability to manage them. In addition, OMB is inserting itself into the decisionmaking process by, for example, requiring EPA to determine five assessments EPA's own Office of Air said that it needed to help implement the Clean Air Act. The effect of all of these changes to what should be a purely scientific process is that chemicals can remain in the assessment process for as much as 10 years and the backlog grows.

Our report included specific recommendations for streamlining in the IRIS program, improving the transparency and credibility of its assessments and ensuring that EPA has the requisite independence to achieve its goals, recommendations that EPA in responding to our March 2008 report agreed to consider. However, when EPA released its new IRIS process in April 2008, we were extremely disappointed.

The new IRIS process is not responsive to our recommendations and in many respects is worse than the draft process we reviewed for our report. For example, the draft process would have made comments from other federal agencies part of the public record. The new process expressly defines such comments as deliberative, excluding them from public scrutiny in what amounts to a black box. As a result, the first assessment drafts to become publicly available are provided to independent peer review committees incorporate undisclosed changes from federal agencies such as the Departments of Defense and Energy, the very agencies that may be affected by the assessments should they lead to regulatory actions. You cannot on one hand preach sound science and on the other hand violate one of its principles: transparency.

Mr. Chairman, you will hear EPA say later in this hearing that the IRIS process is transparent because final assessments must undergo public and external peer review. However, in our view, transparency at this late stage after OMB and other agencies have had multiple opportunities to influence the content of the assessment without any disclosure of their input does not compensate for its absence earlier. Instead of streamlining IRIS, EPA has institutionalized the process that from the outset will take 6 to 8 years to complete a chemical assessment. Under those time frames, the scientific assessments will be obsolete before they can be completed.

To illustrate how bad the situation is, my testimony includes several examples of dangerous chemicals that are stuck in the endless loop of assessment and reassessment. For example, trichloroethylene, or TCE, is a chemical degreasing agent that has been linked to cancer and birth defects since 1995. It is the most commonly occurring contaminant in groundwater today and it is used widely by many including the Department of Defense. EPA initiated a scientific risk assessment of TCE in 1998. EPA's Science Advisory Board completed its peer review and released the assessment for public comment in 2002. DOD and others questioned the assessment and requested a National Academies of Science Review. The Academies concluded its review in 2006 and found that the weight of scientific evidence of cancer from TCE had actually strengthened since the EPA's original assessment. So after more than 10 years, EPA's TCE risk assessment is back to the drawing board and is still not complete and won't be until 2010. In frustration, five Senators who heard about TCE contamination in the drinking water at Camp Lejeune introduced a bill last year that would require EPA to issue final IRIS values and a drinking water standard within 18 months.

Mr. Chairman, as we stated in our March 2008 report, IRIS is a critical process that is clearly broken and needs to be fixed. In order to maintain the integrity of the IRIS process, EPA must streamline its lengthy assessment process and adopt transparency practices that provide assurances that IRIS assessments are appropriately based on the best available science and are not inappropriately based on the policy considerations of OMB and other federal agencies that have a vested interest in the results.

That concludes the summary of my statement, and I will be happy to take questions at the appropriate time.

[The prepared statement of Mr. Stephenson follows:]

United States Government Accountability Office

GAO

Testimony

Before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives

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EPA SCIENCE

New Assessment Process Further Limits the Credibility and Timeliness of EPA's Assessments of Toxic Chemicals

Statement of John B. Stephenson, Director
Natural Resources and Environment

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Highlights

Highlights of GAO-08-1168T, testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives

September 18, 2008

EPA SCIENCE

New Assessment Process Further Limits the Credibility and Timeliness of EPA's Assessments of Toxic Chemicals

Why GAO Did This Study

The Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) contains EPA's scientific position on the potential human health effects of exposure to more than 540 chemicals. Toxicity assessments in the IRIS database constitute the first two critical steps of the risk assessment process, which in turn, provides the foundation for risk management decisions. Thus, IRIS is a critical component of EPA's capacity to support scientifically sound environmental decisions, policies, and regulations.

This testimony discusses (1) highlights of GAO's March 2008 report, *Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System*; (2) key aspects of EPA's revised IRIS assessment process, released on April 10, 2008; and (3) progress EPA has made in completing assessments in fiscal year 2008. For the March 2008 report, GAO reviewed and analyzed EPA data and interviewed officials at relevant agencies, including the Office of Management and Budget (OMB). For this testimony, GAO supplemented the prior audit work with a review of EPA's revised IRIS assessment process announced on April 10, 2008. We also updated our information on EPA's assessment productivity through September 12, 2008.

To view the full product, including the scope and methodology, click on GAO-08-1168T. For more information, contact John Stephenson at (202) 512-3841 or stephensonj@gao.gov.

What GAO Found

In March 2008, GAO concluded that the IRIS database was at serious risk of becoming obsolete because EPA had not been able to complete timely, credible assessments or decrease its backlog of 70 ongoing assessments—a total of 4 were completed in fiscal years 2006 and 2007. In addition, assessment process changes EPA had recently made, as well as other changes EPA was considering at the time of GAO's review, would further reduce the credibility and timeliness of IRIS assessments. We concluded the following:

- EPA's efforts to finalize assessments have been thwarted by a combination of factors, including two new OMB-required reviews of IRIS assessments by OMB and other federal agencies and by EPA management decisions, such as delaying some assessments to await new research.
- The two new OMB/interagency reviews of draft assessments involve other federal agencies in EPA's IRIS assessment process in a manner that limits the credibility of IRIS assessments and hinders EPA's ability to manage them. For example, the OMB/interagency reviews lack transparency, and OMB required EPA to terminate five assessments EPA had initiated to help it implement the Clean Air Act.
- The changes to the IRIS assessment process that EPA was considering, but had not yet issued at the time of our review, would have added to the already unacceptable level of delays in completing IRIS assessments and further limited the credibility of the assessments.

EPA issued its revised IRIS assessment process in April 2008. The new process is largely the same as the draft GAO evaluated and does not respond to the recommendations in GAO's March 2008 report. Moreover, some key changes are likely to further exacerbate the productivity and credibility concerns GAO identified. For example, while the draft process would have made comments from other federal agencies on IRIS assessments part of the public record, EPA's new process defines such comments as "deliberative" and excludes them from the public record. GAO continues to believe that it is critical that input from all parties—particularly agencies that may be affected by the outcome of IRIS assessments—be publicly available. In addition, the estimated time frames under the new process, especially for chemicals of key concern, will likely perpetuate the cycle of delays to which the majority of ongoing assessments have been subject. Instead of streamlining the process, as GAO recommended, EPA has institutionalized a process that from the outset is estimated to take 6 to 8 years. This is problematic because of the substantial rework such cases often require to take into account changing science and methodologies.

EPA's progress in completing assessments continues to be slow—only four assessments have been completed in fiscal year 2008. Further, these assessments cover a group of four related chemicals that were processed and peer reviewed together but finalized individually. Little or no progress has been made on assessments of chemicals highlighted in our report, including naphthalene, formaldehyde, and trichloroethylene (TCE).

Mr. Chairman and Members of the Subcommittee:

I am pleased to be here today to discuss issues associated with the credibility and usefulness of the Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) as the Subcommittee examines scientific integrity at the agency. Containing EPA's scientific position on the potential human health effects that may result from exposure to more than 540 chemicals in the environment, IRIS is one of the most significant tools that EPA has developed to effectively support its mission of protecting people and the environment from harmful chemical exposures. IRIS is therefore a critical component of EPA's capacity to support scientifically sound risk management decisions, policies, and regulations.

As shown in figure 1, the toxicity assessments in the IRIS database fulfill the first two critical steps of the National Academies'[1] four-step risk assessment process—providing hazard identification and quantitative dose-response assessments. IRIS information can then be used with the results of exposure assessments (typically conducted by EPA's program or regional offices) to provide an overall characterization of the public health risks for a given chemical in a given situation. The development of health risk assessments is thus directly dependent on the development of toxicity assessments such as those developed in the IRIS program.

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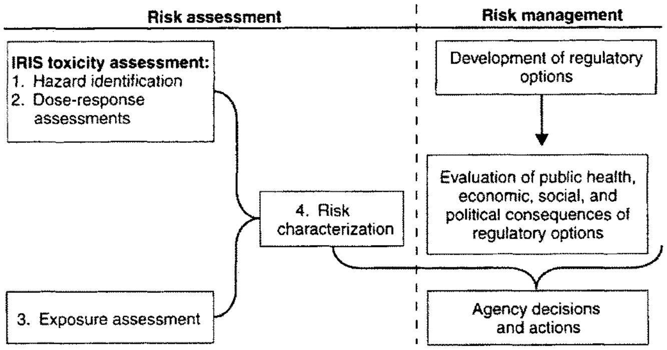
[1] The National Academies comprises four organizations: the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council.

Figure 1: National Academies' Risk Assessment and Risk Management Model Used by EPA


Risk assessment
Risk management
IRIS toxicity assessment:
1. Hazard identification
2. Dose-response assessments
4. Risk characterization
3. Exposure assessment
Development of regulatory options
Evaluation of public health, economic, social, and political consequences of regulatory options
Agency decisions and actions

Source: National Academies.

Under the National Academies' risk assessment and risk management paradigm, policy considerations become relevant in the risk management phase, which occurs after the risk assessment phase. With risk assessment information, decision makers can make informed risk management decisions on how to protect public health, reflecting other important data and considerations, such as the costs and benefits of mitigating identified risks, the technological feasibility of managing risks, and the concerns of various stakeholders. Examples of risk management decisions include deciding how much of a chemical a company may discharge into a river, determining the extent to which a hazardous waste site must be cleaned up, and setting allowable levels of contamination in drinking water.

Thus, although IRIS assessments are not regulatory in nature, the quantitative IRIS values are likely to influence many risk management decisions and serve as a basis for regulatory consideration. However, EPA's productivity in finalizing IRIS assessments is poor, and EPA has a significant backlog of incomplete IRIS assessments and a growing number of outdated assessments. Importantly, EPA has not been able to complete assessments of key chemicals of concern to public health, including dioxin, formaldehyde, trichloroethylene (TCE), naphthalene, and tetrachloroethylene (perc) (see app. I).

In this context, my testimony today discusses (1) highlights of our March 2008 report, *Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System*,[2] (2) key aspects of EPA's revised IRIS assessment process, released on April 10, 2008,[3] and (3) progress EPA has made in completing assessments in fiscal year 2008. For our March 2008 report, we examined the outcome of steps EPA has taken to ensure that IRIS contains current, credible chemical risk information; to address the backlog of ongoing assessments; and to respond to new requirements from the Office of Management and Budget (OMB). We also examined the potential effects of planned changes to the IRIS assessment process on EPA's ability to ensure that IRIS provides current, credible risk information. In conducting our work, we obtained and analyzed information on EPA's productivity and the resources provided to the program for fiscal years 2000 through 2007, user needs, and EPA's assessment completion goals. We also interviewed EPA's National Center for Environmental Assessment officials who manage the IRIS assessment program; officials from other EPA program offices and federal science and health agencies involved in the IRIS assessment process; and officials from the Department of Defense, the Department of Energy (DOE), the National Aeronautics and Space Administration (NASA), and OMB. We have supplemented our report with a review of the IRIS assessment process that EPA released on April 10, 2008, and with updated information on the status of EPA's IRIS assessments. We conducted this work from September 11 to September 18, 2008, in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

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[2] GAO-08-440 (Washington, D.C.: Mar. 7, 2008).

[3] See *Toxic Chemicals: EPA's New Assessment Process Will Increase Challenges EPA Faces in Evaluating and Regulating Chemicals*, GAO-08-743T (Washington, D.C.: Apr. 29, 2008) and *Chemical Assessments: EPA's New Assessment Process Will Further Limit the Productivity and Credibility of Its Integrated Risk Information System*, GAO-08-810T (Washington, D.C.: May 21, 2008).

Background

IRIS was created in 1985 to help EPA develop consensus opinions within the agency about the health effects of chronic exposure to chemicals. Its importance has increased over time as EPA program offices and the states have increasingly relied on IRIS information in making environmental protection decisions. Currently, the IRIS database contains assessments of more than 540 chemicals. According to EPA, national and international users access the IRIS database approximately 9 million times a year. EPA's Assistant Administrator for the Office of Research and Development has described IRIS as the premier national and international source for qualitative and quantitative chemical risk information; other federal agencies have noted that IRIS data are widely accepted by all levels of government across the country for application of public health policy, providing benefits such as uniform, standardized methods for toxicology testing and risk assessment, as well as uniform toxicity values. Similarly, a private-sector risk assessment expert has stated that the IRIS database has become the most important source of regulatory toxicity values for use across EPA's programs and is also widely used across state programs and internationally.

Historically and currently, the focus of IRIS toxicity assessments has been on the potential health effects of long-term (chronic) exposure to chemicals. According to OMB, EPA is the only federal agency that develops qualitative and quantitative assessments of both cancer and noncancer risks of exposure to chemicals, and EPA does so largely under the IRIS program. Other federal agencies develop quantitative estimates of noncancer effects or qualitative cancer assessments of exposure to chemicals in the environment. While these latter assessments provide information on the effects of long-term exposures to chemicals, they provide only qualitative assessments of cancer risks (known human carcinogen, likely human carcinogen, etc.) and not quantitative estimates of cancer potency, which are required to conduct quantitative risk assessments.

EPA's IRIS assessment process has undergone a number of formal and informal changes during the past several years. While the process used to develop IRIS chemical assessments includes numerous individual steps, or activities, major assessment steps include (1) a review of the scientific literature; (2) preparation of a draft IRIS assessment; (3) internal EPA reviews of draft assessments; (4) two OMB/interagency reviews, managed by OMB, that provide input from OMB as well as from other federal agencies, including those that may be affected by the IRIS assessments if they lead to regulatory or other actions; (5) an independent peer review conducted by a panel of experts; and (6) the completion of a final assessment that is posted to the IRIS Web site.

Unlike many other EPA programs that have statutory requirements, including specific time frames for completing mandated tasks, the IRIS program is not subject to statutory requirements or time frames. In contrast, the Department of Human Health and Services' Agency for Toxic Substances and Disease Registry (ATSDR), which develops quantitative estimates of the noncancer effects of exposures to chemicals in the environment, is statutorily required to complete its assessments within certain time frames.

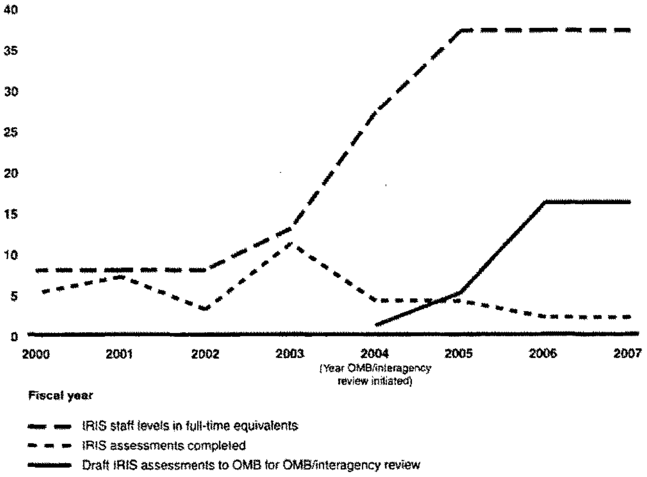
Findings and Recommendations from Our March 2008 Report on the Credibility and Usefulness of EPA's Integrated Risk Information System

The IRIS database is at serious risk of becoming obsolete because the agency has not been able to routinely complete timely, credible assessments or decrease a backlog of 70 ongoing assessments. Specifically, although EPA has taken important steps to improve the IRIS program and productivity since 2000 and has developed a number of draft assessments for external review, its efforts to finalize the assessments have been thwarted by a combination of factors including the imposition of external requirements, the growing complexity and scope of risk assessments, and certain EPA management decisions. In addition, the changes to the IRIS assessment process that EPA was considering at the time of our review would have added to the already unacceptable level of delays in completing IRIS assessments and further limited the credibility of the assessments.

EPA's Efforts to Improve the IRIS Assessment Program Have Not Produced the Desired Results

EPA has taken a number of steps to help ensure that IRIS contains current, credible chemical risk information; to address its backlog of ongoing assessments; and to respond to new OMB requirements. However, to date, these changes—including increasing funding, centralizing staff conducting assessments, and revising the assessment process—have not enabled EPA to routinely complete credible IRIS assessments or decrease the backlog. That is, although EPA sent 32 draft assessments for external review in fiscal years 2006 and 2007, the agency finalized only 4 IRIS assessments during this time (see fig. 2).

Figure 2: Number of Completed IRIS Assessments, Draft Assessments to OMB, and IRIS Staff in Full-Time Equivalents, Fiscal Years 2000-2007



Source: GAO analysis of EPA data

Several key factors have contributed to EPA's inability to achieve a level of productivity that is needed to sustain the IRIS program and database: new OMB-required reviews of IRIS draft assessments by OMB and other federal agencies; the growing complexity and scope of risk assessments; certain EPA management decisions and issues, including delaying completion of some assessments to await new research or to develop enhanced analyses of uncertainty in the assessments; and the compounding effect of delays. Regarding the last factor, even a single delay in the assessment process can lead to the need to essentially repeat the assessment process to take into account changes in science and methodologies.

A variety of delays have impacted the majority of the 70 assessments being conducted as of December 2007—48 had been in process for more than 5 years, and 12 of those for more than 9 years. These time frames are problematic because of the substantial rework such cases often require to take into account changing science and methodologies before they can be completed. For example, EPA's assessment of the cancer risks stemming from exposure to naphthalene—a chemical used in jet fuel and in the production of widely used commercial products such as moth balls, dyes, insecticides, and plasticizers—was nearing completion in 2006. However, prior to finalizing this assessment, which had been ongoing for over 4 years, EPA decided that the existing noncancer assessment had become outdated and essentially restarted the assessment to include both cancer and noncancer effects. As a result, 6 years after the naphthalene assessment began, it is now back at the drafting stage. The assessment now will need to reflect relevant research completed since the draft underwent initial external peer review in 2004, and it will have to undergo all of the IRIS assessment steps again, including the additional internal and external reviews that are now required (see app. I).

Further, because EPA staff time continues to be dedicated to completing assessments in the backlog, EPA's ability to both keep the more than 540 existing assessments up to date and initiate new assessments is limited. Importantly, EPA program offices and state and local entities have requested assessments of hundreds of chemicals not yet in IRIS, and EPA data as of 2003 indicated that the assessments of 287 chemicals in the database could be outdated—that is, new information could change the risk estimates currently in IRIS or enable EPA to develop additional risk estimates for chemicals in the database (for example, developing a cancer potency estimate for assessments with only noncancer estimates). In addition, because EPA's 2003 data are now more than 4 years old, it is likely that more assessments may be outdated now.

The consequences of not having current, credible IRIS information can be significant. EPA's inability to complete its assessment of formaldehyde, which the agency initiated in 1997 to update information already in IRIS on the chemical, has had a significant impact on EPA's air toxics program. Although in 2003 and 2004, the National Cancer Institute and the National Institute of Occupational Safety and Health (NIOSH) had released updates to major epidemiological studies of industrial workers that showed a relationship between formaldehyde and certain cancers, including leukemia, EPA did not move forward to finalize an IRIS assessment incorporating these important data. Instead, EPA opted to await the results of another update to the National Cancer Institute study. While this additional research was originally estimated to take, at most, 18 months to complete, at the time of our report (more than 3 years later) the update was not complete. In the absence of this information, EPA's Office of Air and Radiation decided to use risk information developed by an industry-funded organization—the CIIT Centers for Health Research—for a national emissions standard. This decision was a factor in EPA's exempting certain facilities with formaldehyde emissions from the national emissions standard. The CIIT risk estimate indicates formaldehyde's potency at about 2,400 times lower than the estimate in IRIS that was being re-evaluated and that did not yet consider the 2003 and 2004 National Cancer Institute and NIOSH epidemiological studies. According to an EPA official, an IRIS cancer risk factor based on the 2003 and 2004 National Cancer Institute and NIOSH studies would likely be close to the current IRIS assessment, which EPA has been re-evaluating since 1997. The discrepancy between these two risk estimates raises concerns about whether the public health is adequately protected in the absence of current IRIS information. For example, in 1999, EPA published a national assessment that provided information about the types and amounts of air toxics to which people are exposed. The assessment, which also used the CIIT risk estimate for formaldehyde, concluded, for example, that formaldehyde did not contribute significantly to the overall cancer risk in the state of New Jersey. However, in carrying out its own risk assessment on formaldehyde, the New Jersey Department of Environmental Protection opted to use the risk information that is currently in IRIS (dating back to 1991) and found that the contribution from formaldehyde to overall cancer risk in New Jersey is quite significant, second only to diesel particulate matter. (App. I provides additional information on EPA's IRIS assessment for formaldehyde.)

One of the factors that has contributed to EPA's inability to complete assessments in a timely manner—the new OMB-directed OMB/interagency review process—also limits the credibility of the assessments because it lacks transparency. Specifically, neither the comments nor the changes EPA makes to the scientific IRIS assessments in response to the comments made by OMB and other federal agencies, including those whose workload and resource levels could be affected by the assessments, are disclosed. In addition, the OMB/interagency reviews have hindered EPA's ability to independently manage its IRIS assessments. For example, without communicating its rationale for doing so, OMB directed EPA to terminate five IRIS assessments that for the first time addressed acute, rather than chronic exposure—even though EPA initiated this type of assessment to help it implement the Clean Air Act.

The Expansion of Agencies' Roles in IRIS Assessments That EPA Was Considering at the Time of Our Review Would Have Caused Further Delays and Limited the Assessments' Credibility

For our March 2008 report, we reviewed the additional assessment process changes EPA was planning and concluded that they would likely exacerbate delays in completing IRIS assessments and further affect their credibility. Specifically, despite the OMB/interagency review process that OMB required EPA to incorporate into the IRIS assessment process in 2005, certain federal agencies continued to believe they should have greater and more formal roles in EPA's development of IRIS assessments. Consequently, EPA had been working for several years to establish a formal IRIS assessment process that would further expand the role of federal agencies in the process—including agencies such as DOD, which could be affected by the outcome of IRIS assessments. For example, some of these agencies and their contractors could face increased cleanup costs and other legal liabilities if EPA issued an IRIS assessment for a chemical that resulted in a decision to regulate the chemical to protect the public. In addition, the agencies could be required to, for example, redesign systems and processes to eliminate hazardous materials; develop material substitutes; and improve personal protective clothing, equipment, and procedures. Under the changes that EPA was planning at the time of our review, these potentially affected agencies would have the opportunity to be involved, or provide some form of input, at almost every step of EPA's IRIS assessment process. Most significantly, the changes would have provided federal agencies, including those facing potential regulatory liability, with several opportunities during the IRIS assessment process to subject particular chemicals of interest to additional process steps. These additional process steps, which would have lengthened assessment times considerably, include

- giving federal agencies and the public 45 days to identify additional information on a chemical for EPA's consideration in its assessment or to correct any errors on an additional assessment draft that would provide qualitative information;[4]
- giving potentially affected federal agencies 30 days to review the public comments EPA received and initiate a meeting with EPA if they want to discuss a particular set of comments;
- allowing potentially affected federal agencies to have assessments suspended for up to 18 months to fill a data gap or eliminate an uncertainty factor that EPA plans to use in its assessment; and
- allowing other federal agencies to weigh in on (1) the level of independent peer review that would be sought (that is, whether the peer reviews would be conducted by EPA Science Advisory Board panels, National Academies' panels, or panels organized by an EPA contractor); (2) the areas of scientific expertise needed on the panel; and (3) the scope of the peer reviews and the specific issues they would address.

EPA estimated that assessments that undergo these additional process steps would take up to 6 years to complete. While it is important to ensure that assessments consider the best science, EPA has acknowledged that waiting for new data can result in substantial harm to human health, safety, and the environment. Further, although coordination with other federal agencies about IRIS assessments could enhance their quality,[5] increasing the role of agencies that may be affected by IRIS assessments in the process itself reduces the credibility of the assessments if that expanded role is not transparent. In this regard, while EPA's proposed changes would have allowed for including federal agencies' comments in the public record, the implementation of this proposal was delayed for a year, in part, because of OMB's view that agencies' comments about IRIS assessments represent internal executive branch communications that may not be made public—a view that is inconsistent with the principle of sound science, which relies on, among other things, transparency. (App. II and III provide flow charts of the IRIS process that was in place at the time of our review and EPA's draft proposed process being considered at the time of our review, respectively).

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[4] This represents an additional review of a new draft product and comment period that had not existed previously. As shown in app. II, the assessment process EPA used at the time of our review included publishing its annual IRIS assessment agenda in the *Federal Register* and soliciting relevant scientific information from the public.

[5] We recommended in our 2006 report on human health risk assessment that EPA consistently involve stakeholders as appropriate to the risk assessment. We made this recommendation in the context of improving the overall quality, consistency, and transparency of risk assessments. GAO, *Human Health Risk Assessment: EPA Has Taken Steps to Strengthen Its Process, but Improvements Needed in Planning, Data Development, and Training*, GAO-06-595 (Washington, D.C.: May 31, 2006).

Recommendations Made in Our March 2008 Report

To address the productivity and credibility issues we identified, we recommended that the EPA Administrator require the Office of Research and Development to re-evaluate its draft proposed changes to the IRIS assessment process in light of the issues raised in our report and ensure that any revised process, among other things, clearly defines and documents an IRIS assessment process that will enable the agency to develop the timely chemical risk information it needs to effectively conduct its mission. One of our recommendations—that EPA provide at least 2 years' notice of IRIS assessments that are planned—would, among other things, provide an efficient alternative to suspending assessments while waiting for new research because interested parties would have the opportunity to conduct research before assessments are started.
In addition, we recommended that the EPA Administrator take steps to better ensure that EPA has the ability to develop transparent, credible IRIS assessments—an ability that relies in large part on EPA's independence in conducting these important assessments. Actions that are key to this ability include ensuring that EPA can (1) determine the types of assessments it needs to support EPA programs and (2) define the appropriate role of external federal agencies in EPA's IRIS assessment process, and (3) manage an interagency review process in a manner that enhances the quality, transparency, timeliness, and credibility of IRIS assessments. In its February 21, 2008, letter providing comments on our draft report, EPA said it would consider each of our recommendations in light of the new IRIS process the agency was developing.

Key Aspects of the Revised IRIS Assessment Process Implemented in April 2008 Which Is Not Responsive to Our Recommendations

On April 10, 2008, EPA issued a revised IRIS assessment process, effective immediately. Overall, EPA's revised process is not responsive to the recommendations made in our March 2008 report—it is largely the same as the draft proposed process we evaluated in our March 2008 report (see app. III and IV). Moreover, changes EPA did incorporate into the final process are likely to further exacerbate the productivity and credibility issues we identified in our report.

- *We recommended that EPA ensure that, among other things, any revised process clearly defines and documents a streamlined IRIS assessment process that can be conducted within time frames that minimize the need for wasteful rework.*

  As discussed in our report, when assessments take longer than 2 years, they can become subject to substantial delays stemming from the need to redo key analyses to take into account changing science and assessment methodologies. However, EPA's revised process institutionalizes a process that the agency estimates will take up to 6 years to complete. Further, the estimated time frames do not factor in the time for peer reviews conducted by the National Academies, which can take 2 years to plan and complete.[6] EPA typically uses reviews by the National Academies for highly controversial chemicals or complex assessments. Therefore, assessments of key chemicals of concern to public health that are reviewed by the National Academies are likely to take at least 8 years to complete. These time frames must also be considered in light of OMB's view that health assessment values in IRIS are out of date if they are more than 10 years old and if new scientific information exists that could change the health assessment values. Thus, EPA's new process institutionalizes time frames that could essentially require the agency to start assessment updates as soon as 2 years after assessments are finalized in order to keep the IRIS database current. Such time frames are not consistent with our recommendation that EPA develop, clearly define, and document a streamlined IRIS process that can be conducted within time frames that minimize the need for wasteful rework. Further, the agency would need a significant increase in resources to support such an assessment cycle.

  In addition, EPA had previously emphasized that, in suspending assessments to allow agencies to fill in data gaps, it would allow no more than 18 months to complete the studies and have them peer reviewed. However, under the new process, EPA states that it *generally* will allow no more than 18 months to complete the studies and have them peer reviewed. As we concluded in our report, we believe the ability to suspend assessments for up to 18 months would add to the already unacceptable level of delays in completing IRIS assessments. Further, we and several agency officials with whom we spoke believe that the time needed to plan, conduct, and complete research that would address significant data gaps, and have it peer reviewed, would likely exceed 18 months. Therefore, the less rigid time frame EPA included in its new process could result in additional delays.

Finally, the new process expands the scope of one of the additional steps that initially was to apply only to chemicals of particular interest to federal agencies.[7] Specifically, under the draft process we reviewed, EPA would have provided an additional review and comment opportunity for federal agencies and the public for what EPA officials said would be a small group of chemicals. However, under EPA's new process, this additional step has been added to the assessment process for all chemicals and, therefore, will add time to the already lengthy assessments of all chemicals.

- *We also recommended that the EPA Administrator take steps to better ensure that EPA has the ability to develop transparent, credible IRIS assessments—an ability that relies in large part on EPA's independence in conducting these important assessments.*

Contrary to our recommendation, EPA has formalized a revised IRIS process that is selectively, rather than fully, transparent, limiting the credibility of the assessments. Specifically, while the draft process we reviewed provided that comments on IRIS assessments from OMB and other federal agencies would be part of the public record,

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[6] It is not clear whether the time frames exclude reviews conducted by EPA's Science Advisory Board, which can also add considerably more time than the most basic level of peer review used by the IRIS program—panels organized by an EPA contractor.

[7] The new IRIS assessment process refers to such chemicals as "mission critical." The process defines a mission-critical chemical as one that "is an integral component to the successful and safe conduct of an agency's mission in any or all phases of its operations." According to the process, "impacts on the use of mission-critical chemicals include cessation or degradation of the conduct of the mission and/or unacceptable resource constraints."

under the recently implemented process, comments from federal agencies are expressly defined as "deliberative" and will not be included in the public record.[8] Given the importance and sensitivity of IRIS assessments, we believe it is critical that input from all parties, particularly agencies that may be affected by the outcome of IRIS assessments, be publicly available. However, under EPA's new process, input from some IRIS assessment reviewers—representatives of federal agencies, including those facing potential regulatory liability, and private stakeholders associated with these agencies—will continue to receive less public scrutiny than comments from all others.

In commenting on a draft of our March 2008 report, and in a recent congressional hearing, EPA's Assistant Administrator, Office of Research and Development, stated that the IRIS process is transparent because all final IRIS assessments must undergo public and external peer review. However, as we stated in our report, the presence of transparency at a later stage of IRIS assessment development does not explain or excuse its absence earlier. Under the new process, neither peer reviewers nor the public are privy to the changes EPA makes in response to the comments OMB and other federal agencies provide to EPA at several stages in the assessment process—changes to draft assessments or to the questions EPA poses to the peer review panels. Importantly, the first IRIS assessment draft that is released to peer reviewers and to the public includes the undisclosed input from federal agencies potentially subject to regulation and therefore with an interest in minimizing the impacts of IRIS assessments on their budgets and operations.

In addition, EPA's revised process does not provide EPA with sufficient independence in developing IRIS assessments to ensure they are credible and transparent. We made several recommendations aimed at restoring EPA's independence. For example, we recommended that the EPA Administrator ensure that EPA has the ability to, among other things, define the appropriate role of external federal agencies in the IRIS assessment process and determine when interagency issues have been appropriately addressed. However, under the newly implemented IRIS assessment process, OMB

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[8] Making these comments public would have been a change from the OMB/interagency review process that has been in place since 2004.

> continues to inform EPA when EPA has adequately addressed OMB's and interagency comments. This determination must be made both before EPA can provide draft assessments to external peer reviewers and to the public and before EPA can finalize and post assessments on the IRIS database. While EPA officials state that ultimately IRIS assessments reflect EPA decisions, the new process does not support this assertion given the clearances EPA needs to receive from OMB to move forward at key stages. In fact, we believe the new IRIS assessment process may elevate the goal of reaching interagency agreement above achieving IRIS program objectives. Further, as discussed above, because the negotiations over OMB/interagency comments are not disclosed, whether EPA is entirely responsible for the content of information on IRIS is open to question.

In our report, we also emphasized the importance of ensuring that IRIS assessments be based solely on science issues and not policy concerns. However, under the new IRIS assessment process, EPA has further introduced policy considerations into the IRIS assessment process. That is, the newly implemented IRIS assessment process broadens EPA's characterization of IRIS assessments from "the agency's scientific positions on human health effects that may result from exposure to environmental contaminants" to "the agency's science and science policy positions" on such effects. EPA's new, broader characterization of IRIS raises concerns about the agency's stated intent to ensure that scientific assessments are appropriately based on the best available science and that they are not inappropriately impacted by policy issues and considerations. For example, in discussing science and science policy at a recent Senate hearing, EPA's Assistant Administrator of Research and Development described science policy considerations as including decisions about filling knowledge gaps (e.g., whether and to what extent to use default assumptions) and assessing weight-of-the-evidence approaches to make scientific inferences or assumptions. We believe that these are scientific decisions that should reflect the best judgment of EPA scientists who are evaluating the data, using the detailed risk assessment guidance the agency has developed for such purposes. We have concerns about the manner and extent to which other federal agencies, including those that may be affected by the outcome of assessments, are involved in these decisions as well as the lack of transparency of their input. As we highlighted earlier, under the National Academies' risk assessment and risk management paradigm, policy considerations are relevant in the risk management phase—which occurs *after* the risk assessment phase that encompasses IRIS assessments. The National Academies recently addressed this issue as follows: "The committee believes that risk assessors and risk managers should talk with each other; that is, a 'conceptual distinction' does not mean establishing a wall between risk assessors and risk managers. Indeed they should have constant interaction. However, the dialogue should not bias or otherwise color the risk assessment conducted, and the activities should remain distinct; that is, risk assessors should not be performing risk management activities."[9]

EPA's Progress in Completing Assessments in Fiscal Year 2008

EPA's progress in completing assessments continues to be slow—only four final assessments have been completed in fiscal year 2008. Further, these assessments cover four related chemicals within a larger class of chemicals—polybrominated diphenyl ethers—that were processed and peer reviewed together in a single external peer review panel workshop, but finalized as four separate assessments.

Moreover, little or no progress has been made on assessments of the key chemicals highlighted in our report—naphthalene, formaldehyde, Royal Demolition Explosive (RDX), trichloroethylene (TCE), tetrachloroethylene (perc), and 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). At the time of our March 2008 report, all of these assessments, with the exception of tetrachloroethylene, were in the draft development stage. As of September 11, 2008, according to IRIS Track, none of these assessments had moved to the next step—agency review. EPA's current estimates for completing these assessments raise further concerns. For example, at the time of our report, EPA estimated that it would complete the naphthalene assessment in 2009, which would have reflected a total assessment time frame of 7 years. However, since that time, EPA has updated its estimates in IRIS Track, which now indicate that naphthalene will not be completed until November 2011. In addition, EPA does not have any estimate of when it expects to complete three of the assessments—dioxin, RDX, and TCE. The estimated completion dates are listed as "to be determined" for these chemicals. This is particularly concerning for dioxin and TCE, which have already been in progress for over 17 years and over 10 years, respectively.

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[9] National Academies, *Scientific Review of the Proposed Risk Assessment Bulletin from the Office of Management and Budget Committee to Review the OMB Risk Assessment Bulletin* (2007).

Concluding Observations

The new IRIS assessment process that EPA implemented in April 2008 will not allow the agency to routinely and timely complete credible assessments. In fact, it will exacerbate the problems we identified in our March 2008 report and sought to address with our recommendations—all of which were aimed at preserving the viability of this critical database, which is integral to EPA's mission of protecting the public and the environment from exposure to toxic chemicals. Specifically, under the new process, assessment time frames will be significantly lengthened, and the lack of transparency will further limit the credibility of the assessments because input from OMB and other agencies at all stages of the IRIS assessment process is now expressly defined as deliberative and therefore not subject to public disclosure. The position of the Assistant Administrator, Office of Research and Development, that the IRIS process is transparent because all final IRIS assessments must undergo public and external peer review is unconvincing. Transparency at a later stage of the IRIS assessment process—after OMB and other federal agencies have had multiple opportunities to influence the content of the assessment without any disclosure of their input—does not compensate for its absence earlier.

We continue to believe that to effectively maintain IRIS EPA must streamline its lengthy assessment process and adopt transparency practices that provide assurance that IRIS assessments are appropriately based on the best available science and that they are not inappropriately biased by policy issues and considerations. As discussed in our April 29, 2008, testimony before the Senate Environment and Public Works Committee and our May 21, 2008, testimony before the House Subcommittee on Investigations and Oversight, Committee on Science and Technology, we believe that the Congress should consider requiring EPA to suspend implementation of its new IRIS assessment process and develop a streamlined process that is transparent and otherwise responsive to our recommendations aimed at improving the timeliness and credibility of IRIS assessments.[10] For example, suspending assessments to obtain additional research is inefficient; alternatively, with longer-term planning, EPA could provide agencies and the public with more advance notice of assessments, enabling them to complete relevant research before IRIS assessments are started.

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[10] GAO-08-743T and GAO08-810T

In addition, as discussed in our testimonies, the Congress should consider requiring EPA to obtain and be responsive to input from the Congress and the public before finalizing a revised IRIS assessment process. We note that while EPA and OMB initially had planned for EPA to release a draft revised IRIS assessment process to the public, hold a public meeting to discuss EPA's proposed changes, and seek and incorporate public input before finalizing the process, EPA released its new assessment process without obtaining public input and made it effective immediately. This was inconsistent with assertions made in OMB's letter commenting on our draft report, which emphasized that EPA had not completed the development of the IRIS assessment process and stated: "Indeed, the process will not be complete until EPA circulates its draft to the public for comments and then releases a final product that is responsive to those comments."

Finally, if EPA is not able to take the steps we have recommended to effectively maintain this critical program, other approaches, including statutory requirements, may need to be explored.

Mr. Chairman, this concludes my prepared statement. I would be happy to respond to any questions that you or other Members of the Subcommittee may have at this time.

Contacts and Acknowledgments

For further information about this testimony, please contact John B. Stephenson on (202) 512-3841 or stephensonj@gao.gov. Contact points for our Congressional Relations and Public Affairs Offices may be found on the last page of this statement. Contributors to this testimony include Christine Fishkin (Assistant Director), Laura Gatz, Richard P. Johnson, and Nancy Crothers.

Appendix I: Examples of Key IRIS Assessments That Have Been Delayed

Some key IRIS assessments have been in progress for a number of years, in part because of delays stemming from one or more of the key factors we identified that have hindered EPA's productivity.[11] Examples include the following:

Naphthalene. EPA started the IRIS assessment of cancer risks stemming from the inhalation of naphthalene in 2002. Naphthalene is used in jet fuel and in the production of widely used commercial products such as moth balls, dyes, insecticides, and plasticizers. According to a presentation delivered at the 2007 annual meeting of the Society for Risk Analysis by an Army Corps of Engineers toxicologist,[12] "The changing naphthalene regulatory environment includes a draft EPA risk assessment that if/when finalized, will change naphthalene's status from 'possible' to 'likely' human carcinogen."[13] Thus, according to this presentation, one potential impact of this IRIS assessment on DOD is that DOD would need to provide many employees exposed to naphthalene with equipment measuring their exposure to the chemical. In addition, because many military bases are contaminated with naphthalene, a component of jet fuel (approximately 1 percent to 3 percent) used by all DOD services, DOD could face extensive cleanup costs. By 2004, 2 years after starting the assessment, EPA had drafted a chemical assessment that had completed internal peer reviews and was about to be sent to an external peer review committee. Once it returned from external review, the next step, at that time, would have been a formal review by EPA's IRIS Agency Review Committee. If approved, the assessment would have been completed and released. However, in part because of concerns raised by DOD,

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[11] The factors we identified that have hindered EPA's efforts to improve productivity are the OMB/interagency review process managed by OMB, the growing complexity and scope of risk assessments, certain management decisions and issues regarding the IRIS program, congressional action that has delayed some assessments with potentially significant economic effects, and the compounding effect of delays.

[12] Presentations at the Society for Risk Analysis meeting reflect the views of the authors and "do not necessarily reflect the views of any other organization or agency."

[13] Using its 1996 Proposed Guidelines for Carcinogen Risk Assessment, EPA concluded in the 1998 IRIS assessment of naphthalene that its human carcinogenic potential could not be determined at that time, but noted that there was suggestive evidence of potential human carcinogenicity. (EPA also noted that under its 1986 cancer guidelines, EPA classified naphthalene as a possible human carcinogen.) Subsequently, in 2002, the International Agency for Research on Cancer (IARC), part of the World Health Organization, concluded that naphthalene is possibly carcinogenic to humans; in 2004, the Department of Health and Human Services' National Toxicology Program concluded that naphthalene can reasonably be anticipated to be a human carcinogen. EPA's current assessment will be subject to the agency's 2005 cancer guidelines.

OMB asked to review the assessment and conducted an interagency review of the draft. In their 2004 reviews of the draft IRIS assessment, both OMB and DOD raised a number of concerns about the assessment and suggested to EPA that it be suspended until additional research could be completed to address what they considered to be significant uncertainties associated with the assessment. Although all of the issues raised by OMB and DOD were not resolved, EPA continued with its assessment by submitting the draft for external peer review, which was completed in September 2004.[14] However, according to EPA, OMB continued to object to the draft IRIS assessment and directed EPA to convene an additional expert review panel on genotoxicity to obtain recommendations about short-term tests that OMB thought could be done quickly.[15] According to EPA, this added 6 months to the process, and the panel, which met in April 2005, concluded that the research that OMB was proposing could not be conducted in the short term. Nonetheless, EPA officials said that the second expert panel review did not eliminate OMB's concerns regarding the assessment, which they described as reaching a stalemate. In September 2006, EPA decided, however, to proceed with developing the assessment. By this time, the naphthalene assessment had been in progress for over 4 years; EPA decided that the IRIS noncancer assessment, issued in 1998, was outdated and needed to be revisited. Thus, EPA expanded the IRIS naphthalene assessment to include both noncancer and cancer assessments. As a result, 6 years after the naphthalene assessment began, it is now back at the drafting stage. The assessment now will need to reflect relevant research completed since the draft underwent initial external peer review in 2004, and it will have to undergo all of the IRIS assessment steps again, including additional internal and external reviews that are now required. This series of delays has limited EPA's ability to conduct its mission. For example, the Office of Air and Radiation has identified the naphthalene assessment as one of its highest-priority needs for its air toxics program. In addition, the Office of Solid Waste and Emergency Response considers the naphthalene assessment a high priority for the Superfund program—naphthalene has been found in at least 654 of Superfund's current or former National Priorities List sites.[16] At the time of our

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[14] According to DOD, EPA did not specifically ask the peer reviewers to address some of the technical questions DOD had raised and wanted the peer review to address.

[15] Genotoxic substances are a type of carcinogen, specifically those capable of causing genetic mutation and of contributing to the development of tumors. This includes both certain chemical compounds and certain types of radiation.

[16] The National Priorities List is EPA's list of seriously contaminated sites.

March 2008 report, EPA estimated that it would complete the assessment in 2009. The agency has since updated its estimate to reflect a later expected completion date, November 30, 2011.

Royal Demolition Explosive. This chemical, also called RDX or hexahydro-1,3,5-trinitrotriazine, is a highly powerful explosive used by the U.S. military in thousands of munitions. Currently classified by EPA as a possible human carcinogen, this chemical is known to leach from soil to groundwater. Royal Demolition Explosive can cause seizures in humans and animals when large amounts are inhaled or ingested, but the effects of long-term, low-level exposure on the nervous system are unknown. As is the case with naphthalene, the IRIS assessment could potentially require DOD to undertake a number of actions, including steps to protect its employees from the effects of this chemical and to clean up many contaminated sites. Although EPA started an IRIS assessment of Royal Demolition Explosive in 2000, it has made minimal progress on the assessment because EPA agreed to a request by DOD to wait for the results of DOD-sponsored research on this chemical. In 2007, EPA began to actively work on this assessment, although some of the DOD-sponsored research is still outstanding.

Formaldehyde. EPA began an IRIS assessment of formaldehyde in 1997 because the existing assessment was determined to be outdated.[17] Formaldehyde is a colorless, flammable, strong-smelling gas used to manufacture building materials, such as pressed wood products, and used in many household products, including paper, pharmaceuticals, and leather goods. While EPA currently classifies formaldehyde as a probable human carcinogen, the International Agency for Research on Cancer (IARC), part of the World Health Organization, classifies formaldehyde as a known human carcinogen. Since 1986, studies of industrial of workers have suggested that formaldehyde exposure is associated with nasopharyngeal cancer, and possibly with leukemia. For example, in 2003 and 2004, the National Cancer Institute (NCI) and the National Institute of Occupational Safety and Health (NIOSH) released epidemiological studies following up on earlier studies tracking about 26,000 and 11,000 industrial workers, respectively, exposed to formaldehyde; the updates showed exposure to formaldehyde might also cause leukemia in humans, in addition to the cancer types previously identified. According to NCI officials, the key findings in their follow-up study were an increase in leukemia deaths and, more significantly, an exposure/response relationship between formaldehyde and leukemia—as exposure increased, the incidence of leukemia also rose. As with the earlier study, NCI found more cases of a rare form of cancer, nasopharyngeal cancer, than would usually be expected. The studies from NCI and NIOSH were published in 2003 and 2004,[18] around the time that EPA was still drafting its IRIS assessment. In November 2004, the Chairman of the Senate Environment and Public Works Committee requested that EPA delay completion of its IRIS assessment until an update to the just-released NCI study could be conducted, indicating that the effort would take, at most, 18 months. EPA agreed to wait—and almost 4 years later, the NCI update is not yet complete. NCI plans to release the results of its study in two publications—one focused on lymphatic and hematopoietic tumors and effects (including leukemia) and the other focused on other effects they observed (including other cancers). NCI estimates that the manuscript for the first stage may be published by early 2009. The second manuscript will likely not be published until late 2009. An NCI official said that the additional leukemia deaths identified in the update provide "greater power" to detect associations between exposure to formaldehyde and cancer. EPA's inability to complete the IRIS assessment it started more than 10 years ago in a timely manner has had a significant impact on EPA's air toxics program. Specifically, when EPA promulgated a national emissions standard for hazardous air pollutants covering facilities in the plywood and composite wood industries in 2004, EPA's Office of Air and Radiation took the unusual step of not using the existing IRIS estimate but rather decided to use a cancer risk estimate developed by an industry-funded organization, the CIIT Centers for Health Research (formerly, the Chemical Industry Institute of Toxicology) that had been used by the Canadian health protection agency. The IRIS cancer risk factor had been subject to criticism because it was last revised in 1991 and was based on data from the 1980s. In its final rule, EPA stated that "the dose-response value in IRIS is based on a 1987 study, and no longer represents the best available science in the peer-reviewed literature." The CIIT quantitative cancer risk estimate that EPA used in its health risk assessment in the plywood and composite wood national emissions standard indicates a potency about 2,400 times lower than the estimate in IRIS that was being re-evaluated and that did not yet consider the 2003 and 2004 NCI and NIOSH epidemiological studies. According to an EPA official, an IRIS cancer risk factor based on the 2003 and 2004 NCI and NIOSH studies would likely be close to the current IRIS assessment, which EPA has been attempting to update since 1997. The decision to use the CIIT assessment in the plywood national emissions standard was controversial, and officials in EPA's National Center for Environmental Assessment said the center identified numerous problems with the CIIT estimate. Nonetheless, the Office of Air and Radiation used the CIIT value, and that decision was a factor in EPA exempting certain facilities with formaldehyde emissions from the national emissions standard. In June 2007, a federal appellate court struck down the rule, holding that EPA's decision to exempt certain facilities that EPA asserted presented a low health risk exceeded the agency's authority under the Clean Air Act.[19] Further, the continued delays of the IRIS assessment of formaldehyde—currently estimated to be completed at the end of 2009[20] but after almost 11 years still in the draft development stage—will impact the quality of other EPA regulatory actions, including other air toxics rules and requirements.

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[17] The cancer portion of the formaldehyde assessment was originally issued in 1989 and updated in 1991; the noncancer assessment was added in 1990.

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[18] NCI published the results of its study in two publications. The first study, published in November 2003, focused on the association between formaldehyde exposure and leukemia. M. Hauptmann, J. H. Lubin, P. A. Stewart, R. B. Hayes, A. Blair, "Mortality from Lymphohematopoietic Malignancies among Workers in Formaldehyde Industries," *Journal of the National Cancer Institute* (2003). The second study, published in June 2004, evaluated the association between formaldehyde exposure and other cancers—including nasopharyngeal cancer. M. Hauptmann, J. H. Lubin, P. A. Stewart, R. B. Hayes, A. Blair, "Mortality from Solid Cancers among Workers in Formaldehyde Industries," *American Journal of Epidemiology* (2004). The results of the NIOSH study were described in one publication, dated March 2004, which assessed mortality from all causes and all cancers. L. E. Pinkerton, M. J. Hein, L. T. Stayner, "Mortality among a Cohort of Garment Workers Exposed to Formaldehyde: an Update," *Occupational and Environmental Medicine* (2004).

Trichloroethylene. Also known as TCE, this chemical is a solvent widely used as a degreasing agent in industrial and manufacturing settings; it is a common environmental contaminant in air, soil, surface water, and groundwater. TCE has been linked to cancer, including childhood cancer, and other significant health hazards, such as birth defects. TCE is the most frequently reported organic contaminant in groundwater, and contaminated drinking water has been found at Camp Lejeune, a large Marine Corps base in North Carolina. TCE has also been found at Superfund sites and at many industrial and government facilities, including aircraft and spacecraft manufacturing operations. In 1995, the International Agency for Research on Cancer classified TCE as a probable human carcinogen, and in 2000, the Department of Health and Human Services' National Toxicology Program concluded that it is reasonably anticipated to be a human carcinogen. Because of questions raised by peer reviewers about the IRIS cancer assessment for TCE, EPA withdrew it from IRIS in 1989 but did not initiate a new TCE cancer assessment until 1998. In 2001, EPA issued a draft IRIS assessment for TCE that proposed a range of toxicity values indicating a higher potency than in the prior IRIS values and characterizing TCE as "highly likely to produce cancer in humans." The draft assessment, which became controversial, was peer reviewed by EPA's Scientific Advisory Board and released for public comment. A number of scientific issues were raised during the course of these reviews, including how EPA had applied emerging risk assessment methods—such as assessing cumulative effects (of TCE and its metabolites) and using a physiologically based pharmacokinetic model—and the uncertainty associated with the new methods themselves.[21] To help address these issues, EPA, DOD, DOE, and NASA sponsored a National Academies review to provide guidance. The National Academies report, which was issued in 2006, concluded that the weight of evidence of cancer and other health risks from TCE exposure had strengthened since 2001 and recommended that the risk assessment be finalized with currently available data so that risk management decisions could be made expeditiously. The report specifically noted that while some additional information would allow for more precise estimates of risk, this information was not necessary for developing a credible risk assessment. Nonetheless, 10 years after EPA started its IRIS assessment, the TCE assessment is back at the draft development stage. At the time of our March 2008 report, EPA estimated that this assessment would be finalized in 2010. Since that time, EPA has modified the expected completion date to "to be determined." More in line with the National Academies' recommendation to act expeditiously, five senators introduced a bill in August 2007 that, among other things, would require EPA to both establish IRIS values for TCE and issue final drinking water standards for this contaminant within 18 months.

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[19] *Natural Resources Defense Council v. E.P.A.*, 489 F.3d 1364, 1372-73 (D.C. Cir, 2007). The court did not specifically address EPA's reliance on the CIIT study, holding instead that the Clean Air Act prohibited establishment of the exemptions at issue.

Tetrachloroethylene. EPA started an IRIS assessment of tetrachloroethylene—also called perchloroethylene or "perc"—in 1998. Tetrachloroethylene is a manufactured chemical widely used for dry cleaning of fabrics, metal degreasing, and making some consumer products and other chemicals. Tetrachloroethylene is a widespread groundwater contaminant, and the

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[20] At the time of our March 2008 report, EPA estimated that the assessment would not be complete until 2010. The current estimate of 2009 appears optimistic in light of continued delays in the NCI study updates.

Department of Health and Human Services' National Toxicology Program has determined that it is reasonably anticipated to be a carcinogen. The IRIS database currently contains a 1988 noncancer assessment based on oral exposure that will be updated in the ongoing assessment. Importantly, the ongoing assessment will also provide a noncancer inhalation risk and a cancer assessment. The IRIS agency review of the draft assessment was completed in February 2005, the draft assessment was sent to OMB for OMB/interagency review in September 2005, and the OMB/interagency review was completed in March 2006. EPA had determined to have the next step, external peer review, conducted by the National Academies—the peer review choice reserved for chemical assessments that are particularly significant or controversial. EPA contracted with the National Academies for a review by an expert panel, and the review was scheduled to start in June 2006 and be completed in 15 months. However, as of December 2007, the draft assessment had not yet been provided to the National Academies. After verbally agreeing with both the noncancer and cancer assessments following briefings on the assessments, the Assistant Administrator, Office of Research and Development, subsequently requested that additional uncertainty analyses—including some quantitative analyses—be conducted and included in the assessment before the draft was released to the National Academies for peer review. As discussed in our March 2008 report on IRIS (GAO-08-440), quantitative uncertainty analysis is a risk assessment tool that is currently being developed, and although the agency is working on developing policies and procedures for uncertainty analysis, such guidance currently does not exist. At the time of our March 2008 report, we indicated that the draft tetrachloroethylene assessment had been delayed since early 2006 as EPA staff went back and forth with the Assistant Administrator trying to reach agreement on key issues such as whether a linear or nonlinear model was most appropriate for the cancer assessment and how uncertainty should be qualitatively and quantitatively characterized. EPA officials and staff noted that some of the most experienced staff were being used for these efforts, limiting their ability to work on other IRIS assessments. In addition, we noted that the significant delay had impacted the planned National Academies peer review because the current contract, which has already been extended once, cannot be extended beyond December 2008. The peer review was initially estimated to

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[21] Physiologically based pharmacokinetic models are a class of dosimetry models that are useful for predicting internal doses to target organs. With the appropriate data, these models can be used to extrapolate across species and exposure scenarios and address various sources of uncertainty in risk assessments.

take 15 months. Since the time of our March 2008 report, EPA released the draft assessment for public comment and held a "listening session"[22] to receive comments. However, the agency has not yet announced a date or a location for the external peer review in the *Federal Register*.

Dioxin. The dioxin assessment is an example of an IRIS assessment that has been, and will likely continue to be, a political as well as a scientific issue. Often the byproducts of combustion and other industrial processes, complex mixtures of dioxins enter the food chain and human diet through emissions into the air that settle on soil, plants, and water. EPA's initial dioxin assessment, published in 1985, focused on the dioxin TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) because animal studies in the 1970s showed it to be the most potent cancer-causing chemical studied to date. Several years later, EPA decided to conduct a reassessment of dioxin because of major advances that had occurred in the scientific understanding of dioxin toxicity and significant new studies on dioxins' potential adverse health effects. Initially started in 1991, this assessment has involved repeated literature searches and peer reviews. For example, a draft of the updated assessment was reviewed by a scientific peer review panel in 1995, and three panels reviewed key segments of later versions of the draft in 1997 and 2000. In 2002, EPA officials said that the assessment would conclude that dioxin may adversely affect human health at lower exposure levels than had previously been thought and that most exposure to dioxins occurs from eating such American dietary staples as meats, fish, and dairy products, which contain minute traces of dioxins. These foods contain dioxins because animals eat plants and commercial feed and drink water contaminated with dioxins, which then accumulate in animals' fatty tissue. It is clear that EPA's dioxin risk assessment could have a potentially significant impact on consumers and on the food and agriculture industries. As EPA moved closer to finalizing the assessment, in 2003 the agency was directed in a congressional appropriations conference committee report to not issue the assessment until it had been reviewed by the National Academies. The National Academies provided EPA with a report in July 2006. In developing a response to the report, which the agency is currently doing, EPA must include new studies and risk assessment approaches that did not exist when the assessment was drafted. EPA officials said the assessment will be subject to the IRIS review process once its response to the National Academies' report is drafted. As of 2008, EPA has been developing the dioxin assessment, which has potentially significant health implications for all Americans, for 17 years.

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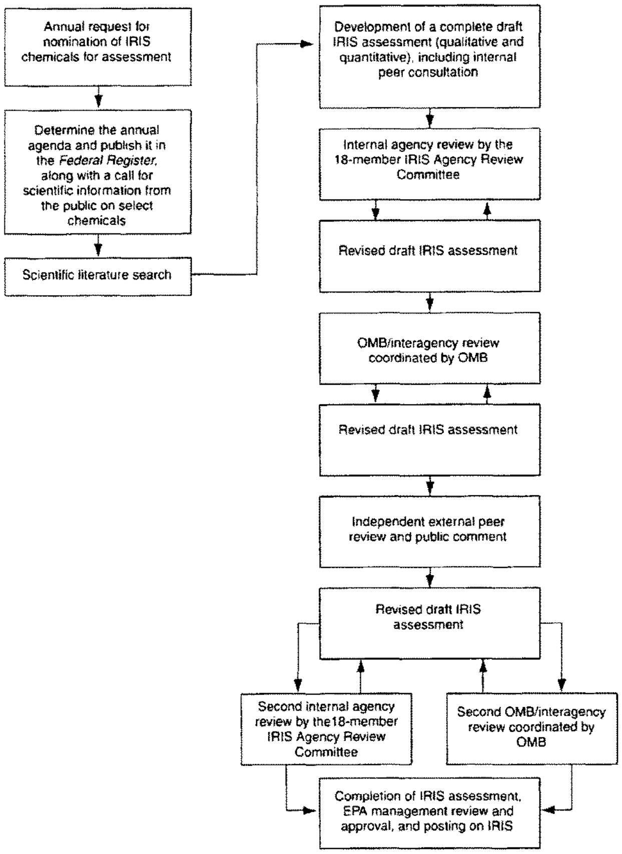
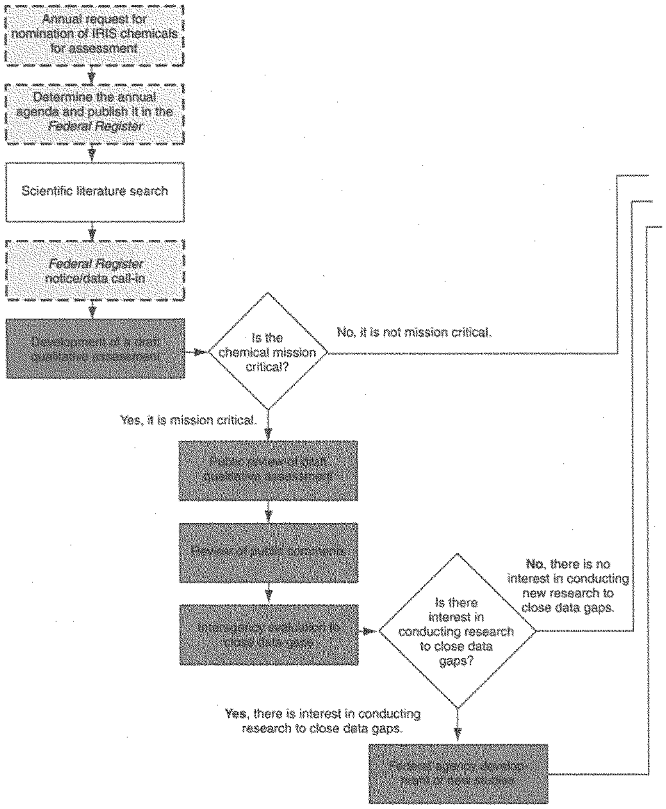
[22] EPA's new assessment process includes a "listening session" open to interested parties that provides interested parties with an opportunity to present scientific and technical comments on draft IRIS health assessments to EPA and other interested parties during a public comment period and prior to the external peer review meeting.

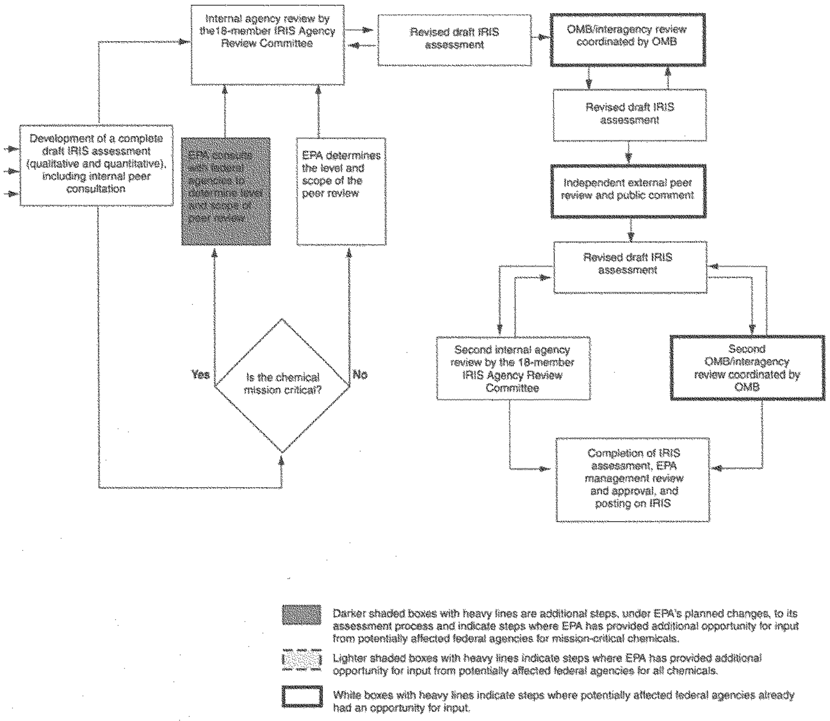
Appendix II: EPA's IRIS Assessment Process Being Implemented at the Time of Our Review (Includes OMB Requirements as of 2005)


Annual request for nomination of IRIS chemicals for assessment
Determine the annual agenda and publish it in the *Federal Register*, along with a call for scientific information from the public on select chemicals
Scientific literature search
Development of a complete draft IRIS assessment (qualitative and quantitative), including internal peer consultation
Internal agency review by the 18-member IRIS Agency Review Committee
Revised draft IRIS assessment
OMB/interagency review coordinated by OMB
Revised draft IRIS assessment
Independent external peer review and public comment
Revised draft IRIS assessment
Second internal agency review by the18-member IRIS Agency Review Committee
Second OMB/interagency review coordinated by OMB
Completion of IRIS assessment, EPA management review and approval, and posting on IRIS

Source: GAO analysis of EPA information.

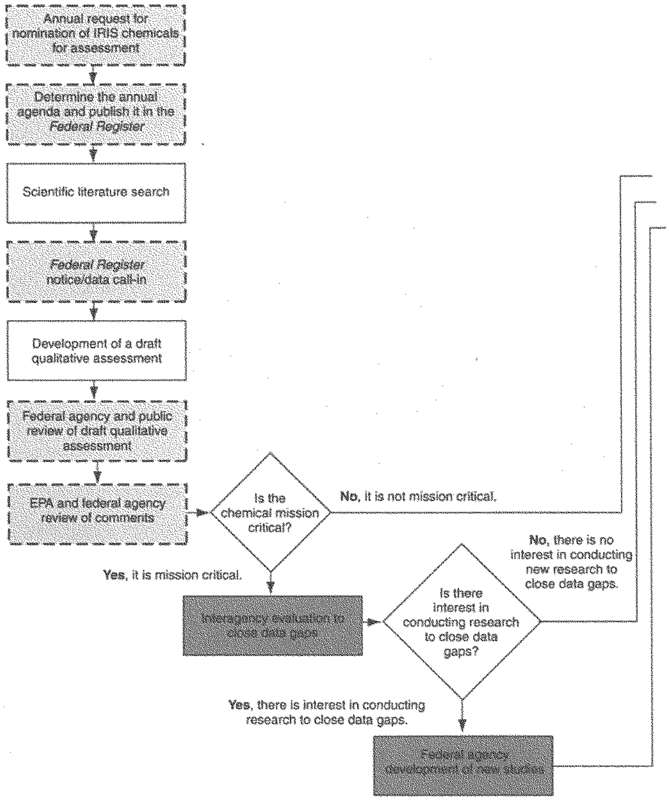
Appendix III: EPA's Draft Proposed IRIS Assessment Process Being Considered at the Time of Our Review (Dated March 2007)

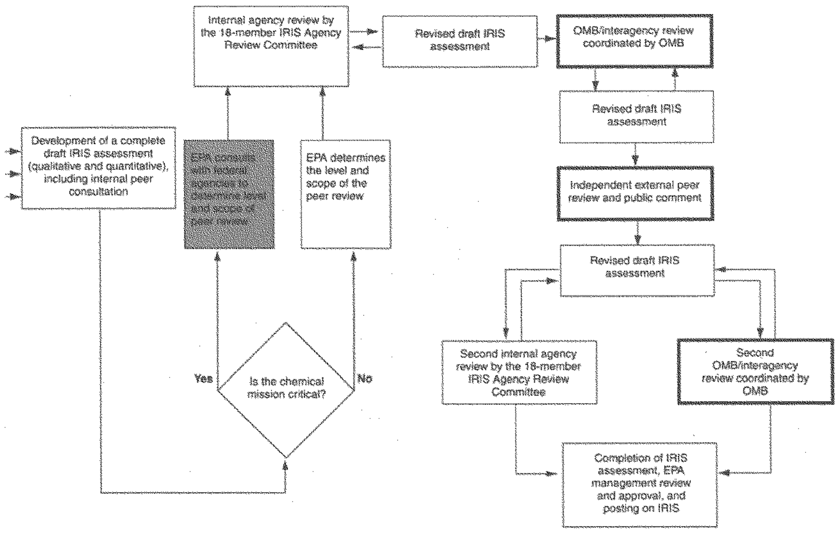

Annual request for nomination of IRIS chemicals for assessment
Determine the annual agenda and publish it in the *Federal Register*
Scientific literature search
Federal Register notice/data call-in
Development of a draft qualitative assessment
Is the chemical mission critical?
No, it is not mission critical.
Yes, it is mission critical.
Public review of draft qualitative assessment
Review of public comments
Interagency evaluation to close data gaps
Is there interest in conducting research to close data gaps?
No, there is no interest in conducting new research to close data gaps.
Yes, there is interest in conducting research to close data gaps.
Federal agency development of new studies


Internal agency review by the18-member IRIS Agency Review Committee
Revised draft IRIS assessment
OMB/interagency review coordinated by OMB
Revised draft IRIS assessment
Development of a complete draft IRIS assessment (qualitative and quantitative), including internal peer consultation
EPA consults with federal agencies to determine level and scope of peer review
EPA determines the level and scope of the peer review
Independent external peer review and public comment
Revised draft IRIS assessment
Yes
Is the chemical mission critical?
No
Second internal agency review by the 18-member IRIS Agency Review Committee
Second OMB/interagency review coordinated by OMB
Completion of IRIS assessment, EPA management review and approval, and posting on IRIS
Darker shaded boxes with heavy lines are additional steps, under EPA's planned changes, to its assessment process and indicate steps where EPA has provided additional opportunity for input from potentially affected federal agencies for mission-critical chemicals.
Lighter shaded boxes with heavy lines indicate steps where EPA has provided additional opportunity for input from potentially affected federal agencies for all chemicals.
White boxes with heavy lines indicate steps where potentially affected federal agencies already had an opportunity for input.

Source: GAO analysis of EPA information.

Appendix IV: EPA's IRIS Assessment Process as of April 10, 2008


Annual request for nomination of IRIS chemicals for assessment
Determine the annual agenda and publish it in the *Federal Register*
Scientific literature search
Federal Register notice/data call-in
Development of a draft qualitative assessment
Federal agency and public review of draft qualitative assessment
EPA and federal agency review of comments
Is the chemical mission critical?
No, it is not mission critical.
Yes, it is mission critical.
Interagency evaluation to close data gaps
Is there interest in conducting research to close data gaps?
No, there is no interest in conducting new research to close data gaps.
Yes, there is interest in conducting research to close data gaps.
Federal agency development of new studies


Internal agency review by the 18-member IRIS Agency Review Committee
Revised draft IRIS assessment
OMB/interagency review coordinated by OMB
Revised draft IRIS assessment
Development of a complete draft IRIS assessment (qualitative and quantitative), including internal peer consultation
EPA consults with federal agencies to determine level and scope of peer review
EPA determines the level and scope of the peer review
Independent external peer review and public comment
Revised draft IRIS assessment
Yes
Is the chemical mission critical?
No
Second internal agency review by the 18-member IRIS Agency Review Committee
Second OMB/interagency review coordinated by OMB
Completion of IRIS assessment, EPA management review and approval, and posting on IRIS

▨ Darker shaded boxes are additional steps under EPA's changes to its assessment process and indicate where EPA has provided additional opportunity for input from potentially affected federal agencies for mission-critical chemicals.

⬚ Lighter shaded boxes with dotted lines indicate steps where EPA has provided additional opportunity for input from potentially affected federal agencies for all chemicals.

☐ White boxes with heavy lines indicate steps where potentially affected federal agencies already had an opportunity for input.

Source: GAO analysis of EPA information.

(361010)

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Mr. STUPAK. Thank you, Mr. Stephenson.

Dr. Grifo.

STATEMENT OF FRANCESCA GRIFO, PH.D., SENIOR SCIENTIST, DIRECTOR, SCIENCE INTEGRITY PROGRAM, UNION OF CONCERNED SCIENTISTS

Ms. GRIFO. Good morning. I am a senior scientist and the director of the Scientific Integrity Program at the Union of Concerned Scientists, a leading science-based nonprofit working for a healthy environment and a safer world. Thank you, Chairmen Stupak and Dingell, Ranking Members Barton and Shimkus, and members of the subcommittee for the opportunity to speak to you this morning about the problem of political interference in science. I thank the Committee for your oversight and I strongly urge you to keep the pressure on. I fear long-lasting consequences from both the abuses of science we have documented and perhaps more so from those abuses still cloaked in secrecy.

The United States has enjoyed prosperity and health in large part because of its strong and sustained commitment to independent science. As the Nation faces new challenges at home and growing competitiveness abroad, the need for a robust federal scientific enterprise remains critical. Unfortunately, political interference in federal science threatens this legacy. Allowing agencies who may be the source of toxic chemicals greater control over the scientific information in EPA's own toxicological database and withholding interagency correspondence about these scientific assessments from public view is emblematic of the problem of manipulation, suppression, and distortion of science at EPA.

While I am sure we can all agree that the Environmental Protection Agency has a skilled and dedicated set of public servants that comprise its workforce, our research based on a UCS census, not a poll—polls and censuses have very distinct methodologies—conducted by Iowa State University including responses from 1,586 scientists, combined with essays from 850 of those scientists, forces us to conclude that this is a troubled agency. Hundreds of scientists reported direct interference in their scientific work and fears of retaliation and systemic disregard for the expertise of EPA's advisory committees. Their good work is compromised by the inappropriate influence of political appointees at the EPA and other agencies as well as commercial and other non-governmental interests.

This influence takes the following forms: scientists being told to exclude or alter technical information in an EPA scientific document; scientists being told to provide incomplete, inaccurate, or misleading information to the public; selective or incomplete use of data to justify a specific outcome; changes or edits that change the meaning of scientific findings; disappearance or unusual delay in the release of scientific information; statements by EPA officials that misrepresent scientists' findings; and lack of a coherent and consistent EPA policy that allows scientists to speak freely to the news media about their research findings.

Our study found that 889 scientists reported personally experiencing one of these events in the last 5 years. In essay responses, nearly 100—and we didn't ask them the question, this came freely, voluntarily—EPA scientists identified OMB as the primary culprit in this interference. Hundreds of scientists reported being unable to openly express concerns about EPA's mission-driven work without fear of retaliation. The percentage of scientists reporting political interference was highest at headquarters and at the four program offices with regulatory responsibilities: Office of Air and Radiation, Office of Prevention, Pesticides and Toxic Substances, and the Office of Solid Waste and Emergency Response. The National Center for Environmental Assessment ranked amongst the worst in the Office of Research and Development.

A bipartisan Congress passed 12 pieces of legislation that authorized the Environmental Protection Agency to protect human health and the environment. By suppressing, distorting, and manipulating science, the White House has subverted this mission, making an end run around the legislative branch. Congress must work closely with the next occupants of the White House, whoever they may be, to ferret out and address the changes that undermine robust science and its application to our Nation's health and environment. When agencies that would be liable for costly cleanups of environmental poisons are given expanded influence over EPA's scientific assessments of chemical toxicity, the public loses.

Fortunately, this is not a problem without a solution. The EPA should increase openness in its decisionmaking process. If research results and analysis by EPA scientists are made public before they drop into the black box of OMB, attempts to distort science will be exposed. The expanded reach of the Office of Management and Budget must be pushed back. Questioning the scientific consensus of agency experts is not the proper role for the Office of Management and Budget. The GAO should identify changes that have become embedded in the Agency that if not exposed will continue to harm scientific integrity. For example, what has been the impact of centralization of power in the White House on EPA decisionmaking? What needs to be done to reverse centralization and restore scientific integrity? How many agency employees are signing non-disclosure agreements and why? Are there decisions where political interference has been exposed that require an immediate review or reversal? All important questions.

Finally, there are three actions that can and must happen immediately. The House and Senate overwhelmingly approved bipartisan legislation to strengthen whistleblower protections for federal employees. It is crucial that the negotiations between the two houses come to a close, producing final legislation that contains strong, specific protections for scientists who expose efforts to suppress or alter federal research. EPA should adopt media, communication and scientific publication policies that ensure taxpayer-funded scientists and their research are accessible, and the scientists at the Agency should be proactively made aware of these rights.

And last but not least, just as former EPA Administrator William Ruckelshaus did 25 years ago, Administrator Johnson should pledge to operate EPA in a fishbowl. The fishbowl memo, which set the standard for an agency so open that it regained the trust of the American people, was reaffirmed by several subsequent EPA administrators. The original memo, still in the history section of EPA's Web site, should be moved front and center to its home page.

We look forward to continuing our work with Congress to restore scientific integrity to federal policymaking. Thank you.

[The prepared statement of Ms. Grifo follows:]

Written Testimony of Francesca T. Grifo, Ph.D.
Senior Scientist with the Union of Concerned Scientists
Director of the Scientific Integrity Program

Before the U.S. House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

"Science Under Siege: Scientific Integrity at the Environmental Protection Agency"

September 18, 2008

This testimony is presented by Dr. Francesca Grifo, Senior Scientist with the Union of Concerned Scientists (UCS), a leading science-based nonprofit working for a healthy environment and a better world. The full testimony is submitted for the record and Dr. Grifo will summarize her statement for the Committee on the problem of political interference in the work of federal government scientists.

Good morning, my name is Dr. Francesca Grifo. I am a Senior Scientist and the Director of the Scientific Integrity Program at the Union of Concerned Scientists, a leading science-based nonprofit working for a healthy environment and a safer world. I would like to thank Chairmen Dingell and Stupak, Ranking Members Barton and Shimkus, and the Members of the Committee for the opportunity to speak to you this morning about the problem of political interference in the work of federal government scientists.

This written testimony contains a brief introduction (p. 1), an overview of the issue of scientific integrity (p. 3), a summary of the report *Interference at the EPA: Politics and Science at the U.S. Environmental Protection Agency* released April 23, 2008 (p. 6), further analysis of political interference in the EPA decisions relating to toxic chemicals (p. 11), a summary of reforms needed to restore scientific integrity to the federal policy making process (p. 15) and some concluding thoughts (p. 21). Also included are a timeline of abuses of science compiled by UCS (p. 22), selected essay responses from UCS's survey of EPA scientists (p. 25), a statement on *Scientific Freedom and the Public Good* endorsed by many prominent scientists (p. 30), and brief summaries of four past surveys of federal government scientists conducted by UCS (p. 31).

I. Introduction

The United States has enjoyed prosperity and health in large part because of its strong and sustained commitment to independent science. As the nation faces new challenges at home and growing competitiveness abroad, the need for a robust federal scientific enterprise remains critical. Unfortunately an epidemic of political interference in federal science threatens this legacy, promising serious and wide-ranging consequences.

The U.S. Environmental Protection Agency (EPA) has been especially harmed by political interference in its work to protect human health and the environment. Our report documents changes in EPA policies regarding risk assessments that allow polluting federal agencies more control over the science, as well as reductions in the amount of information provided to the public about toxic chemicals in their communities.

These and other EPA decisions based on tainted science have consequences for the health and safety of Americans that can be measured in numbers of hospital visits and premature deaths.[1] The White House has also rewritten EPA scientific documents concerning climate change and pressured EPA scientists to support predetermined conclusions regarding mercury pollution.

To assess the breadth and depth of political interference at the EPA, and to give voice to the thousands of civil servant scientists working at the agency, the Union of Concerned Scientists (UCS) distributed a 44-question survey to nearly 5,500 scientists at the EPA in the summer of 2007 and received responses from 1,586 scientists. The results of that survey, as well as additional investigations, are contained in our recently released report *Interference at the EPA: Politics and Science at the U.S. Environmental Protection Agency.*[2] We summarize here the problems with scientific integrity across the federal government, the major findings of this latest report and outline the solutions needed to restore scientific integrity to federal decision making.

Political interference has penetrated deeply into the culture and practices of federal agencies. This interference in science threatens our nation's ability to respond to complex challenges to public health, the environment, and national security. It risks demoralizing the federal scientific workforce and raises the possibility of lasting harm to the federal scientific enterprise. It betrays public trust in our government and undermines the democratic principles upon which this nation was founded. The thousands of scientists in the employ of the federal government represent a tremendous resource and their knowledge and advice should not be manipulated or ignored. Without strong action to restore integrity to federal science our nation will be ill-prepared to deal with the challenges we face.

II. Scientific Integrity

Successful application of science has played a large part in the policies that have made the United States of America the world's most powerful nation and its citizens increasingly prosperous and healthy.

Although scientific input to the government is rarely the only factor in public policy decisions, scientific input should always be weighted from an objective and impartial perspective. Presidents and administrations of both parties have long adhered to this principle in forming and implementing policies. However, the current Bush administration has consistently undermined this legacy by manipulating, censoring and suppressing the work of federal government scientists—with serious consequences for our health, safety, and environment.

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[1] Scientific papers documenting the health effects of particulate matter and ozone air pollution are numerous and citations for a number of such studies are collected in the following documents: Shprentz, D. 2007. Top ten ozone studies: Public testimony on EPA's proposed revisions to the national ambient air quality standard for ozone. August 30. Online at http://www.cleanairstandards.org/article/2007/08/743; American Lung Association. 2005. Adverse health effects of particulate matter: New science shows effects below current standards. Online at http://www.cleanairstandards.org/article/2005/06/395.

[2] To read the text of the report and see supporting materials go to http://www.ucsusa.org/EPAscience/.

Misrepresenting and suppressing scientific knowledge for political purposes can have serious consequences. For example, if the Nixon administration suppressed air quality studies and vetoed the Clean Air Act of 1970, Americans would have suffered more than 200,000 premature deaths and millions of cases of respiratory and cardiovascular disease over the next 20 years.[3]

This misuse of science has led Russell Train, the EPA administrator under Presidents Nixon and Ford, to observe: "How radically we have moved away from regulation based on independent findings and professional analysis of scientific, health and economic data by the responsible agency to regulation controlled by the White House and driven primarily by political considerations."[4]

Political interference in the work of federal scientists has become widespread in the past several years. To catalog these abuses, UCS launched the *A-to-Z Guide to Political Interference in Science* (see p. 18)[5] a webpage that now documents 85 case studies of such interference, involving 24 government agencies. In our February 2008 report, *Federal Science and the Public Good*,[6] we outlined the patterns of interference with government science. The report also highlights the deeper systemic changes that have been made to the structure and policies of the executive branch that threaten to enshrine politicized science even after George W. Bush leaves office. These findings are summarized below.

Patterns of Abuse

Specific examples of the misuse of science have occurred across a broad range of issues such as childhood lead poisoning, toxic mercury emissions, climate change, reproductive health, and nuclear weapons. Experts at the FDA charged with ensuring the safety of our food and drug supply, report being pressured to alter their scientific conclusions. Political appointees in the Department of the Interior have been exposed for overruling the scientific consensus and refusing to protect endangered species. Scientists nominated to serve on scientific advisory boards report being asked about their political leanings. And scientists studying what may very well be the most profound global change of this century – global warming – are effectively barred from communicating their findings to the news media and the public.

Interference can take many different forms, including:

- Falsifying data and fabricating results. Federal officials with little or no scientific background have misrepresented scientific data and presented scientific results not based on actual research.

- Selectively editing reports and creating false uncertainty. Political appointees have selectively deleted evidence from scientific documents, and exaggerated uncertainty in scientific findings.

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[3] See http://www.epa.gov/oar/sect812. See also data from the American Meteorological Society, online at http://ametsoc.org/sloan/cleanair/index.html.
[4] Train, R. 2003. "E.P.-Eh?" Grist Magazine, September 23.
[5] See http://www.ucsusa.org/AtoZ/.
[6] To read the text of the report go to http://www.ucsusa.org/scientific_integrity/restoring/federal-science.html.

- Tampering with scientific procedures. Federal agencies have replaced standard scientific procedures with flawed methodologies, biased toward finding predetermined results.

- Intimidating and coercing scientists. High-level administration officials have directly pressured researchers at federal agencies to alter scientific findings, threatening reprisal if they refuse.

- Censoring and suppressing scientists. Federal officials have prevented scientists from communicating with their colleagues, the media, and the public.

- Hiding, suppressing, and delaying release of scientific findings. Federal officials have buried scientific findings and prevented their public release.

- Disregarding legally mandated science. Federal agencies have repeatedly ignored scientific research that by law must form the basis for certain policy decisions.

- Allowing conflicts of interest. Officials with clear conflicts of interest have held key positions throughout the federal government, from which they have made decisions harming the integrity of federal science.

- Corrupting scientific advisory panels. Political interests have manipulated the process for selecting members of independent scientific advisory panels.

Changing the Rules

Beyond the system-wide epidemic of interference, the Bush administration has instituted deeper changes in the structure and policies of the executive branch. Without a strong commitment to scientific integrity from the next president and Congress, these changes may ensure that politicization of science will continue after President Bush leaves office.

- Centralizing decision making and the unitary executive. The Bush administration has invoked the theory of the "unitary executive" to justify tight White House control over federal agencies. For example, President Bush has greatly expanded the use of signing statements. He has used them to assert his right to ignore or disobey any laws or requests he considers unconstitutional, including congressional requests for scientific information and whistle-blower rights for federal employees. Executive order 13422 dramatically expands the role of the Office of Management and Budget (OMB) in reviewing all agency regulations, including the scientific basis for regulations.

- Homogenizing agency decision making. The White House has sought to replace the policies of individual agencies regarding peer review of scientific findings, risk assessment, and cost-benefit analysis with inappropriate government-wide standards, ignoring the reality that each federal agency requires different tools to best fulfill its mission.

- Reducing transparency. The Bush administration has limited government transparency and accountability by preventing public disclosure of information on the internal workings of the federal government. New policies regarding Freedom of Information Act requests and classification of government documents have created a "presumption of secrecy." In this approach, agencies automatically keep information from public view unless someone specifically requests it, or the law requires them to disclose it.

- Adding unnecessary bureaucracy. New demands, including interagency review and excessive legal challenges from industry, have prevented federal agencies from acting promptly to protect public health and safety.

- Retaliating against whistle-blowers. The Bush administration's penchant for secrecy and centralizing executive power has increased the vulnerability of federal employees who blow the whistle on government waste, fraud, or abuse.

- Foxes guarding the henhouse. The revolving door for officials who shuttle between high-level government positions and regulated industries has harmed the integrity of federal science. The legacy of political appointees with conflicts of interest lives on in the agencies after their departure—through both the flawed policies they helped enact and the erosion of public trust in agency integrity.

- Removing science from decision making. Administration officials have often simply shut out scientists and scientific information from the policy discussion.

- Weakening enforcement and monitoring. Many federal agencies have seen their ability to enforce the nation's laws decline under the Bush administration. In many cases, agencies are simply not collecting the data they need to ensure robust enforcement.

Scientist Surveys

To move beyond anecdotes and to gather information about the extent and nature of the interference, UCS has conducted a series of surveys of federal scientists. Previous surveys have given voice to scientists at the Fish and Wildlife Service, the National Ocean and Atmospheric Administration Fisheries, the Food and Drug Administration and climate scientists working in seven federal agencies.[7] The survey of EPA scientists is the fifth in the series.

Collectively 3,400 federal government scientists responded to these five surveys. Several common themes ran through their responses:

- 1301 scientists across nine federal agencies reported that they fear retaliation for openly expressing their concerns about the mission driven work of their agencies.
- 688 scientists from four agencies reported that they were not able to publish work in peer reviewed journals if it did not adhere to agency policies.
- 150 federal climate scientists from seven agencies personally experienced at least one incident of political interference in the past five years.
- And from our most recent report, 889 EPA scientists personally experienced at least one incident of inappropriate interference in their work over the past five years.

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[7] More information about the surveys can be found at http://www.ucsusa.org/surveys/.

Scientists Respond

The scientific community has responded to this growing problem. The more than 15,000 individual scientists, including 52 Nobel Laureates and nearly 200 members of the National Academies, who have called for a restoration of scientific integrity in federal policy making have been joined by several major scientific associations, including the American Association for the Advancement of Science, the American Public Health Association, the American Geophysical Union, and the Ecological Society of America, which have addressed the problem at society wide meetings and have begun to investigate how to defend science.

III. Interference at the EPA

The U.S. Environmental Protection Agency (EPA) has the simple yet profound charge "to protect human health and the environment." EPA scientists apply their expertise to protect the public from air and water pollution, clean up hazardous waste, and study emerging threats such as global warming. Because each year brings new and potentially toxic chemicals into our homes and workplaces, because air pollution still threatens our public health, and because environmental challenges are becoming more complex and global, a strong and capable EPA is more important than ever.

Yet challenges from industry lobbyists and some political leaders to the agency's decisions have too often led to the suppression and distortion of the scientific findings underlying those decisions—to the detriment of both science and the health of our nation. While every regulatory agency must balance scientific findings with other considerations, policy makers need access to the highest-quality scientific information to make fully informed decisions.

Concern over this problem led the Union of Concerned Scientists (UCS) to investigate political interference in science at the EPA. In the summer of 2007, UCS, working with the Center for Survey Statistics and Methodology at Iowa State University, distributed a 44-question survey to nearly 5,500 EPA scientists, asking for information about political interference in their scientific work, the use of science in EPA decision making, barriers to communication, employee morale, and the agency's effectiveness. UCS identified these scientists through EPA websites, consultations with current and former employees, and targeted Internet searches.

We received completed surveys from 1,586 scientists, for a response rate of 29 percent. These respondents represented every scientific program office at EPA headquarters, all 10 regional offices, and more than a dozen research laboratories across the country. Most respondents were agency veterans, with more than a decade of experience at the EPA. Beyond specific survey questions, more than 850 scientists also provided written comments in response to an open-ended essay question. To add to this information, UCS interviewed dozens of current and former EPA scientists.

The results of these investigations show an agency under siege from political pressures. On numerous issues—ranging from mercury pollution to groundwater contamination to climate change—political appointees of the George W. Bush administration have edited scientific documents, manipulated scientific assessments, and generally sought to undermine the science behind dozens of EPA regulations.

These findings highlight the need for strong reforms to protect EPA scientists, make agency decision making more transparent, and reduce politicization of the regulatory process.

Political Interference in Scientific Work

Large numbers of EPA scientists reported widespread and inappropriate interference by EPA political appointees, the White House, and other federal agencies in their scientific work:

- 889 scientists (60 percent of respondents[8]) personally experienced at least one incident of political interference during the past five years.

- Among EPA veterans (scientists with more than 10 years experience at the agency), 409 (43 percent) said interference occurred more often in the past five years than in the previous five-year period.

EPA scientists also reported personally experiencing specific forms of political interference, from the explicit to the subtle:

- 94 scientists (7 percent) had frequently or occasionally been "directed to inappropriately exclude or alter technical information from an EPA scientific document."

- 191 scientists (16 percent) had personally experienced frequent or occasional "situations in which scientists have actively objected to, resigned from, or removed themselves from a project because of pressure to change scientific findings."

- 232 scientists (18 percent) had personally experienced frequent or occasional "changes or edits during review that change the meaning of scientific findings."

- 285 scientists (22 percent) had personally experienced frequent or occasional "selective or incomplete use of data to justify a specific regulatory outcome."

- 153 scientists (13 percent) had personally experienced frequent or occasional "pressure to ignore impacts of a regulation on sensitive populations."

- 299 scientists (24 percent) had personally experienced frequent or occasional "disappearance or unusual delay in the release of websites, press releases, reports, or other science-based materials."

- 394 scientists (31 percent) had personally experienced frequent or occasional "statements by EPA officials that misrepresent scientists' findings."

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[8] Unless otherwise stated, percentages reflect the share of respondents who answered a specific question.

Respondents indicated that political interference arose from both internal and external sources:

- 516 scientists (43 percent) knew of "many or some" cases where EPA political appointees had inappropriately involved themselves in scientific decisions.

- 560 scientists (49 percent) knew of "many or some" cases where political appointees at other federal agencies had inappropriately involved themselves in decisions.

- 507 scientists (42 percent) knew of "many or some" cases where "commercial interests have inappropriately induced the reversal or withdrawal of EPA scientific conclusions or decisions through political intervention."

- 329 scientists (28 percent) knew of such interference by "nongovernmental or advocacy groups."

In essay responses, nearly 100 scientists identified the White House Office of Management and Budget (OMB), which oversees the federal budget and coordinates all federal regulations, as the primary source of external interference.

Respondents reported widespread respect for their direct supervisors, but had fewer commendations for EPA's senior leaders:

- 1,282 scientists (81 percent) respected the integrity and professionalism of their direct manager or supervisor, while 686 (43 percent) said the same about EPA's senior leaders.

- A majority of respondents (906 scientists, or 59 percent) agreed that their direct supervisor stands behind scientific staff who express politically controversial opinions.

Rates of political interference varied widely among offices and divisions within the agency:

- The percentage of scientists reporting interference was highest in the program offices with regulatory duties, and at EPA headquarters. A total of 337 scientists in the program offices (68 percent), and 379 scientists at headquarters (69 percent), reported at least one incident of interference in the past five years.

- The percentage of scientists reporting interference was lower—although still significant—in the Office of Research and Development (ORD), the EPA's main research arm. The ORD's National Health and Environmental Effects Research Laboratory was notably freer of interference (39 percent) than any other EPA division, while its National Center for Environmental Assessment had the highest percentage of scientists reporting interference of all EPA divisions (84 percent).

- The percentages of scientists reporting interference in the 10 regional offices varied widely, from 44 percent (region 6) to 73 percent (region 9).

To place these results in context, we cite specific incidents of interference. For example, political appointees at the White House and in top positions at the EPA manipulated scientific findings and analyses regarding mercury pollution and climate change. These incidents involved pressure to change scientific methods and findings, direct editing of scientific documents by nonscientists, and delayed release of scientific reports.

A third case—involving interagency review of the EPA's assessment of toxic chemicals—illustrates the growing ability of the OMB and other federal agencies to review and second-guess the work of the EPA's scientific experts.

Barriers to the Free Communication of Science

The free communication of scientific results is a critical part of the scientific process. Despite statements by EPA leaders asserting that the agency supports scientific openness, many scientists report that it restricts free communication of the results of taxpayer-funded research:

- 783 scientists (51 percent) disagreed or strongly disagreed that EPA policies allow scientists to "speak freely to the news media about their findings." Another 556 scientists (36 percent) had no opinion or were unsure. Only 197 scientists (13 percent) agreed that the EPA allows scientists to communicate freely with the media.

- 291 scientists (24 percent) disagreed or strongly disagreed that they are "allowed to publish work in peer-reviewed scientific journals regardless of whether it adheres to agency policies or positions."

Beyond these restrictive policies, hundreds of scientists said they fear retaliation for speaking candidly about the EPA's work. More scientists feared retaliation for speaking candidly inside the agency than outside it:

- 492 scientists (31 percent) disagreed or strongly disagreed that they could openly express concerns about the EPA's work *inside* the agency without fear of retaliation.

- 382 scientists (24 percent) disagreed or strongly disagreed that they could openly express concerns about the EPA's work *outside* the agency without fear of retaliation.

Interviews with current and former EPA scientists revealed new examples of problems in communicating scientific research. In two cases, EPA scientists were barred from presenting research on climate change at scientific conferences. Other scientists reported difficulties speaking with the media and obtaining EPA clearance to publish their findings in scientific journals.

Political interference in scientific work combined with barriers to the free communication of scientific findings affect the amount and quality of information the U.S. public receives.

Undermining the Role of Science in EPA Decision Making

Scientific information is the lifeblood of much of the EPA's work and the credibility of its decisions depends on the quality of its scientific work. A plurality of EPA scientists reported that the agency's regulatory policies are consistent with its scientific findings. However, a similar number felt that the EPA could do a better job of using the best judgment of its scientific staff:

- 745 scientists (48 percent) felt that the EPA's determinations and actions are frequently or always consistent with the scientific findings in agency documents and reports.

- 719 scientists (47 percent) felt that the EPA's determinations occasionally, seldom, or never make use of the best judgment of its scientific staff.

Hundreds of EPA scientists also felt that the agency only occasionally incorporates expert advice from advisory committees into policy decisions:

- 553 (36 percent) scientists felt that the agency occasionally, seldom, or never heeds advice from independent scientific advisory committees.

Recent changes in the EPA's process for setting the National Ambient Air Quality Standards provide one prominent example of how political considerations have trumped scientific expertise and sidelined EPA's scientific advisory committees.

Challenges to Agency Effectiveness

Beyond political interference in EPA science, several survey questions asked respondents about other factors that could impair their ability to do their jobs, and the ability of the agency as a whole to fulfill its mission. Large numbers of EPA scientists indicated that a lack of sufficient or appropriate resources was a serious issue in their office or division:

- 969 scientists (62 percent) disagreed or strongly disagreed that the "EPA division where I work has sufficient resources to adequately perform its mission of protecting human health and the environment."

- 555 scientists (36 percent) agreed or strongly agreed that the "recent changes and closures in the EPA library system have impaired my ability to do my job." This opinion was especially prevalent among scientists in regions 5, 6, and 7, which had their libraries closed (86 of these scientists, or 48 percent, agreed).

- 574 scientists (41 percent) agreed or strongly agreed that "the trend toward contracting out scientific work is harming the effectiveness of my division."

Survey questions also asked scientists about their job satisfaction, and the morale in their division:

- Respondents were twice as likely to report a decrease in job satisfaction over the past five years as to report an increase (670 versus 328 scientists).

- Opinions about workforce morale ranged widely. A total of 564 scientists (37 percent) said morale was fair, and 387 (25 percent) said morale was poor or extremely poor. A total of 570 scientists (37 percent) said morale was good or excellent.

Questions about the overall effectiveness of the EPA elicited a range of responses:

- Respondents were more likely to agree than disagree that the EPA was acting effectively to clean up environmental problems. A total of 812 scientists (52 percent) agreed that the EPA acts effectively to "clean up and/or mitigate existing pollution or environmental problems," while 522 (33 percent) disagreed.

- 694 scientists (44 percent) agreed that the EPA acts effectively to "foster practices that prevent environmental degradation or adverse health effects before they occur," while 629 scientists (40 percent) disagreed.

- Respondents were twice as likely to report a decrease in the effectiveness of their office or division (696 scientists, or 45 percent) as an increase (321 scientists, or 21 percent) over the past five years.

- Respondents were evenly split on whether the EPA is moving in the right direction. A total of 685 scientists (44 percent) disagreed that EPA is moving in the right direction, while 624 scientists (40 percent) agreed.

IV. Interference in EPA Decisions Regarding Toxic Chemicals

The political interference reported by hundreds of EPA scientists cuts across a wide range of issues, including climate change science, air pollution and water pollution. In this section, we briefly summarize several incidents of political interference in EPA research into toxic chemicals.

IRIS Database

In an April 2008 policy, the EPA announced that it would allow polluting federal agencies greater control over the scientific information in EPA's Integrated Risk Information System (IRIS), a publicly available database containing toxicology profiles of more than 500 chemicals.

Agencies such as the Department of Defense (DOD), the Department of Energy, the Office of Management and Budget (OMB), and the National Aeronautics and Space Administration now have the power to delay or remove chemicals from IRIS review.[9] By classifying chemicals as "mission critical," these agencies can require additional or modified studies on the chemicals. This additional analysis could add years of delay to the release or updating of information on chemicals posing a significant threat to public health. Furthermore, any interagency communications about EPA's scientific assessments are explicitly withheld from public view.[10]

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[9] Inside EPA. 2007a. EPA infighting stalls interagency pact on chemical risk review process. August 17.

[10] U.S. Environmental Protection Agency (EPA). IRIS Process (2008 Update). Online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=190045.

This interagency interference is troubling because federal agencies themselves are part of the regulated community, and thus have significant conflicts of interest in determining the outcome of a toxicity assessment. Recent incidents of outside interference in the IRIS risk assessment process have already delayed and weakened protections for public health, and the 2008 policy will likely institutionalize political meddling in EPA's scientific work.

For example, information from IRIS on the toxicity of perchlorate could mean that the DOD and its contractors are liable for billions of dollars in cleanup costs. The DOD has long sought to weaken any scientific standard that would mandate cleanup of perchlorate contamination.[11] After the EPA's initial 2002 perchlorate assessment, the DOD criticized the EPA's science, and lobbied to have the National Academies review the subject. Air Force Col. Daniel Rogers linked the outcome of scientific deliberations to national security, claiming before the resulting National Academies panel that "every additional layer of science-policy precaution embedded into this risk assessment comes at the expense of the [Defense] Department's ability to acquire and test propulsion and weapons systems."[12] The National Academies panel eventually proposed a perchlorate standard weaker than the EPA's initial risk assessment. The EPA has not yet finalized a drinking water standard for perchlorate.

In another example, the lack of a finalized IRIS assessment for formaldehyde opened the door for OMB and EPA to weaken air pollution standards. Formaldehyde is a cancer-causing gas used to manufacture building materials such as pressed wood.[13] The EPA began an IRIS assessment of formaldehyde in 1997. In 2004 members of Congress requested that the assessment be delayed until the completion of a large epidemiological study from the National Cancer Institute. In the absence of a completed IRIS assessment, the EPA's Office of Air and Radiation relied on a cancer risk assessment provided by an industry-funded organization in drafting its 2004 rule regulating formaldehyde emissions. The industry study found formaldehyde to be 2,400 times less potent than the proposed IRIS value, which was based on robust, peer-reviewed science. This weaker value was used to justify exempting certain plywood and composite wood manufacturing facilities from regulation under the Clean Air Act.[14] The rule was later struck down by a federal court, but the IRIS assessment remains unfinished 11 years after it was begun.

The EPA has also recently proposed that it no longer include numerical assessments of toxicity in its draft reports on IRIS chemicals. This would be a major blow to the public and other regulatory agencies, which often rely on draft reports for information on these chemicals while waiting for the final reports—which can take several years.[15]

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[11] Sass, J. 2004. U.S. Department of Defense and White House working together to avoid cleanup and liability for perchlorate pollution. International Journal of Occupational and Environmental Health 10:330–334. Online at www.ijoeh.com/pfds/1003_Sass.pdf.

[12] Hogue, C. 2003. Scuffle over perchlorate: NAS panel hears agencies' arguments against, for EPA draft risk assessment. Chemical & Engineering News, November 3. Online at http://pubs.acs.org/cen/topstory/8144/8144notw8.html.

[13] ATSDR ToxFAQs for formaldehyde. http://www.atsdr.cdc.gov/tfacts111.html

[14] U.S. Government Accountability Office. Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System. Report to the Chairman, Committee on Environment and Public Works, U.S. Senate. Report No. GAO-08-440; March 2008, p. 37-39. Available at http://www.gao.gov/new.items/d08440.pdf.

Finally, the OMB reviews the "charge" to scientific panels that provide peer review of IRIS risk assessments. The charge determines the questions a panel will answer during its investigation. An independent scientist (name withheld by request) reported that the OMB modified the charge to one such panel by removing questions asking whether the risk assessment adequately addressed public health risks, and adding questions asking if the EPA had gone too far in its risk assessment. The scientist stated that OMB's substitution "served to downplay the risk posed by the chemical in question."[16]

The EPA scientists at the National Center for Environmental Assessment, the office responsible for IRIS and assessing the health risks of toxics, reported the highest levels of interference of any of the EPA centers surveyed. 41 scientists (85% of respondents) reported personally experiencing at least one type of political interference in the last five years.

Toxics Release Inventory

The EPA's Toxics Release Inventory (TRI) requires manufacturers to provide annual reports on their use and release of more than 600 toxic chemicals. The TRI is widely credited with enhancing public knowledge and triggering significant voluntary reductions in emissions of many pollutants. Each year brings dozens of new examples of communities that have relied on the TRI to win protection from dangerous chemicals such as lead, mercury, and chromium.[17] For example, after the Chicago Tribune published TRI data from a local brass foundry, a citizen activist group formed and successfully negotiated protection for residents from extremely high lead levels.[18]

Yet in early 2007 the EPA finalized a plan—known as the TRI burden reduction rule—to scale back reporting requirements by raising the threshold below which facilities are allowed to submit only minimal information.[19] The rule also weakened reporting requirements for the production of persistent toxins that accumulate in plants and animals, such as mercury, lead, and PCBs. The new rule drew widespread criticism for reducing the amount of useful information that the TRI made available to the public.

A 2007 GAO investigation found that the rule disproportionately affected low-income and minority communities, and that the EPA did not conduct the required environmental justice assessment. The GAO also found that the OMB had pressured the EPA to pursue specific policy options that EPA experts had previously discarded, and set an unrealistic deadline, leading to a rushed analysis of the options. The GAO stated that the estimated savings from the rule are

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[15] Inside EPA. 2007b. Administration may halt EPA use of numerical values in draft risk studies. December 14.
[16] Anonymous scientist. 2008. UCS phone interview, March.
[17] Union of Concerned Scientists (UCS). 2006. What toxic chemicals are released in your neighborhood? Online at http://www.ucsusa.org/scientific_integrity/interference/toxic-chemicals-release.html.
[18] Hawthorne, M. 2006. Smelter plans fixes for Pilsen emissions. Chicago Tribune, April 7.
[19] Environmental Protection Agency (EPA). 2006b. Final TRI burden reduction rule, December 18. Washington, DC. Online at http://www.epa.gov/tri/tridata/modrule/phase2/TRIphase2final.pdf.

"likely overstated," and that the EPA's analysis "masked" the large impact the rule would have on communities across the country.[20]

Toxaphene

UCS is concerned that EPA's development of scientific tests for the presence of the pollutant toxaphene inappropriately involved the manufacturer of the contaminant and uses a method that greatly underestimates the concentration of the compound. Such interference may be delaying cleanup of a Superfund site in Georgia with potential to harm the health of the surrounding community.

Toxaphene is a highly toxic pesticide—composed of over 600 different chemicals—manufactured by Hercules, Inc. in Brunswick, Georgia until its ban in the early 1980s.[21] The landfill adjacent to the Hercules chemical plant and the nearby Terry Creek are both National Priority List Superfund sites.[22]

In 1997 the EPA developed a new test for the presence of toxaphene. The testing strategy is accurate in detecting the presence of newly manufactured toxaphene, but underestimates the presence of "weathered toxaphene"—that is, toxaphene that has been present in the environment for years and has broken down into a compound with a different chemical signature. A 2005 report from the EPA's Inspector General found that "EPA's method is a test procedure designed to look for the original, unaltered toxaphene mixture... Unfortunately, EPA's method does not look for, or specifically identify, toxaphene breakdown products."[23] Both the EPA Inspector General and the Agency for Toxic Substances and Disease Registry recommend that the EPA discard the flawed method and adopt testing procedures that measure both toxaphene and its breakdown products.

Of additional concern is the involvement of the original polluter, Hercules, Inc., in the development of these testing procedures in task force meetings dating back to the early 1990s. It is inappropriate for organizations with serious conflicts of interest to be so intimately involved in establishing the testing procedure. UCS has similar concerns about reports that the Weinberg Group (a product defense firm) is involved in designing and carrying out recent tests for toxaphene breakdown products at the site. It would be more appropriate for EPA to convene an official federal advisory committee of scientific experts to develop a rigorous toxaphene testing procedure and to ensure that any organizations with conflicts of interest are excluded.

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[20] Government Accountability Office (GAO). 2007. Toxic chemical releases: EPA actions could reduce environmental information available to many communities. Washington, DC. Online at http://www.gao.gov/new.items/d08128.pdf.

[21] Agency for Toxic Substances and Disease Registry (ATSDR). 2002. Public Health Assessment: Terry Creek Dredge Spoil Areas/Hercules Outfall Site, Bruswick, Glynn County, Georgia. August 12. Online at http://www.atsdr.cdc.gov/HAC/pha/terrycreek/tcd_toc.html.

[22] U.S. EPA. Superfund Site Progress Profile: Terry Creek Dredge Spoil Areas/Hercules Outfall. Online at http://cfpub.epa.gov/supercpad/cursites/csitinfo.cfm?id=0404439.

[23] U.S. EPA, Office of the Inspector General. 2005. Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia. September, 26. Online at http://www.epa.gov/oig/reports/2005/20050926-2005-P-00022.pdf.

Further examples

- Atrazine: Despite compiling hundreds of pages of evidence documenting the harmful effects of atrazine, a commonly used weed killer, the Environmental Protection Agency (EPA) refused to regulate the herbicide. Atrazine has been found to cause severe hormonal damage to wildlife, including amphibians, reptiles and fish. The EPA made its decision following closed-door meetings with the manufacturer. [24]

- Mercury: On March 15, 2005, the EPA issued its final rule regulating mercury emissions from coal-fired power plants. The Clean Air Mercury Rule (CAMR) exempted power plants from standard Clean Air Act rules in favor of a controversial cap-and-trade program. To support this policy decision, political appointees at the White House sought to remove information from an EPA report on children and the environment, instructed EPA scientists to change their analyses to support pre-determined conclusions and included language lifted verbatim from industry memos. In February 2008, a federal appeals court ruled that the CAMR violated the Clean Air Act.[25]

- Selenium: In late 2004, the Environmental Protection Agency (EPA) proposed new selenium standards that scientists say are much too high. The new standards were based on what scientists say was a faulty reading of key research into the effects of selenium on fish populations. Rather than correct its initial misinterpretation of the data, however, the EPA dug in its heels behind new standards that scientists said could be devastating to fragile stream ecosystems.[26]

V. Solutions and Reforms

The results of our survey and interviews with EPA scientists show widespread problems at the agency. Hundreds of scientists report direct and indirect interference with their scientific work by political appointees at the EPA and the White House. Despite claims to the contrary from EPA leaders, scientists also report institutional barriers to freely communicating their findings through both the media and scientific publications. EPA scientists are not confident that environmental decision makers respect their expertise. And the agency's effectiveness needs to improve on several fronts.

Wide-ranging political interference in EPA science requires a suite of reforms in five major arenas: protecting EPA scientists, improving the agency's transparency, reforming its regulatory framework, strengthening its system of scientific advice, and depoliticizing funding, monitoring, and enforcement. These efforts to revitalize the EPA and allowing it to fulfill its mission of protecting human health and the environment will require strong leadership from Congress, the next president, and the next EPA administrator, joined by EPA scientists and the broader scientific community.

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[24] For more information see http://www.ucsusa.org/scientific_integrity/abuses_of_science/atrazine-and-health.html.
[25] For more information see *Interference at the EPA* (UCS 2008), p. 27-32.
[26] For more information see http://www.ucsusa.org/scientific_integrity/abuses_of_science/case_studies_and_evidence/selenium-standards.html.

Protecting EPA Scientists
To fulfill their profound responsibility to the public, EPA scientists need assurance that standing behind their scientific work will not open them to either official or unofficial retaliation. Congress is now considering several bills that would strengthen the federal whistle-blower system:

- Both houses of Congress have passed legislation that would enhance protections for whistle-blowers under the Whistleblower Protection Act of 1989, and members are now working to reconcile the two versions. The House version, H.R. 985, includes specific protections from retaliation for scientists, who expose efforts to distort or suppress federal research. The Senate bill, S. 274, unfortunately, lacks these protections for scientists. It is crucial that these protections are part of the final law now being negotiated by the Senate Homeland Security and Governmental Affairs and the House Oversight and Government Reform Committees.

- Members of the House and Senate have introduced bills to reauthorize the Office of Special Council and the Merit Systems Protection Board—federal entities that investigate claims of reprisal against federal whistleblowers and adjudicate whistleblower claims, respectively. Although the legislation includes many important reforms, the Senate has taken no action, and the House bill is still in committee.

- The House and the Senate have passed legislation to grant greater autonomy to inspectors general (IGs), and immunity from coercion by the agencies they police. Both versions contain an important requirement that IG websites enable employees to anonymously report waste, fraud, and abuse. Government scientists could use this mechanism to confidentially challenge scientific misconduct. Both versions of such legislation also give IGs subpoena power.

Congress should pass the strongest-possible whistle-blower protections, and the president should sign them into law. The next EPA administrator should also work with the coalition of EPA unions to integrate the agency's Principles of Scientific Integrity (EPA 1999) into the official employee grievance procedure.

Making the EPA More Transparent
Some aspects of EPA decision making are open to public scrutiny, but many "predecisional" meetings and discussions are not. The integrity of EPA science is threatened in no small part by decisions made behind closed doors. Opening up these processes to congressional and public scrutiny is an important way to reveal and end abuses of science. The EPA should also better explain how it arrives at decisions that affect health and the environment.

The agency should institute a transparency policy for all meetings attended by non-EPA personnel. Such a policy need not be burdensome to EPA employees: outside participants could enter the required information directly into a database before any meeting, or within a specified time period after a meeting.

- This policy should require the EPA to post all meetings with outside entities on its website, including those with for-profit and not-for-profit organizations, and representatives of other agencies.

- The database should include the names and affiliations of attendees as well as the date, time, location, and subject of each meeting, with an exception granted for cases of national security.

Official EPA reports and documents in draft form are exempt from release under the Freedom of Information Act. Abuse of this exemption—wherein documents remain in draft form indefinitely—does occur.

- To prevent abuse of the "predecisional" exemption, the next EPA administrator should adopt procedures that allow the periodic release of documents that have remained in draft form for a given length of time.

The EPA should also publish a summary statement discussing the scientific basis for any significant policy, guidance, or regulation informed by science. This statement should be available in a timely fashion, and should include:

- The scientific rationale for a decision, and all scientific documents and data used to make it (including reasonable release of information from industry)

- A minority report voicing any significant dissenting scientific evidence or opinions

- An explanation of how the agency resolved such differences of opinion

- Identification by name of each official and employee who participated in the decision.

The Food and Drug Administration Amendments Act of 2007 already incorporates such transparency requirements, and the EPA could adapt them.

Reforming Media Policy

Both science and democracy thrive in an open environment. The EPA should clarify its policies on the interaction between scientists and the media, to ensure that the public has access to taxpayer-funded information that affects their health and safety, and to ensure that scientists and other employees can exercise their rights to free speech:

- Any EPA media policy must respect at least two fundamental rights: (1) scientists have the right to speak freely about any topic (including EPA policy) if they clarify that they are speaking as private citizens, not as agency representatives; and (2) scientists should have the right to review and correct any official document (such as a press release or report) that cites or references their scientific work, to ensure that accuracy has been maintained after the clearance and editing process.

- Congress or the EPA may need to impose narrow restrictions on these basic rights in certain instances, such as in cases under litigation. Officials should clearly define these situations.

- However, because the EPA is also a scientific agency, it should also exceed these basic rights by creating a public affairs system that actively disseminates agency research and codifies the positive rights of EPA scientists.

- The next EPA administrator should review the written policies of all offices and regions on the interaction between agency scientists and the media. Policies that do not explicitly protect scientists' fundamental right to freely communicate their scientific findings should be rewritten, and offices and regions without explicit policies should create them.

- The EPA should hold training sessions to clearly explain employees' rights in communicating their research to the media and the public, and the resources available to them to do so.

Reforming Publication Policy

Peer review is a pillar of the scientific method; political review is not. The EPA's process for clearing information for outside publication sometimes becomes a de facto policy review, and delays publication of controversial papers despite disclaimers that the views are personal.

- The next EPA administrator should review the agency's clearance policies, and work with the agency's offices and divisions to streamline excessive review.

- A disclaimer on a published paper that it is not official agency policy should exempt it from a full policy review.

- The clearance process should set reasonable yet strict time limits on how long the agency can delay publication of a paper. If officials do not reach a decision within that time frame, the paper should automatically proceed to publication with a written disclaimer. If officials deny clearance, they should provide a written explanation to the authors.

- The process for reviewing and clearing papers for outside publication must be transparent, and thus posted on the website of each EPA office and division.

Reforming the Regulatory Process

While the White House oversees federal agencies, it must strike a balance between administration priorities and agency independence. The EPA was created to implement and enforce the nation's environmental laws, and it has developed the expertise, experience, processes, and policies to fulfill those critical duties. The regulatory process should respect the agency's reservoir of scientific and technical knowledge. Congress should also consider ways to strengthen our nation's environmental regulatory system, to fortify the EPA's scientific mission and meet the pressing challenges of the twenty-first century.

Ensuring Agency Independence

The EPA is the nation's first line of defense against threats to public health and the environment. As such, the EPA should be empowered to take the lead on environmental concerns and to push back against interference in its science and decisions by the OMB and other federal agencies. To accomplish this:

- The next president should elevate the EPA to a cabinet-level agency, or establish a Department of the Environment.

- The next president should reverse executive order 13422, removing the power of presidential appointees unaccountable to Congress to commence rulemaking, and returning that power to the EPA and its administrator.

The OMB and its Office of Information and Regulatory Affairs play important roles in coordinating and overseeing the regulatory process. However, those roles should not include second-guessing or editing the science underlying EPA decisions:

- The next president should establish a regulatory process that respects the scientific and technical expertise of the EPA, and that excludes the OMB from interfering in EPA's scientific and technical determinations.

- The next president should repeal the OMB's one-size-fits-all directives on peer review and risk assessment. The EPA should have the flexibility to choose the form of peer review best suited to its needs.

- In particular, EPA experts should prepare risk assessments and the scientific component of regulatory impact assessments without interference from the OMB.

Enacting Legislative Reforms

The dozen or so environmental laws noted in Chapter 2 have led to dramatic improvements in public health and environmental quality. Yet the challenges the nation faces today are very different from those of 30 years ago. Congress should assess the adequacy of our current environmental regulatory structure, and consider reforms to close loopholes and strengthen the EPA's ability to address pressing threats to human health and the environment. (See CPR 2007 for possible recommendations.)

To support the quality of the EPA's scientific work, these reforms should focus on ensuring that the agency has the regulatory tools it needs to collect critical environmental data. Such tools could include stronger scientific testing requirements for pesticides and chemicals used in commerce, expanded TRI reporting requirements, and the authority to broaden environmental monitoring networks where necessary.

Congress should also consider new legislation that gives the EPA a framework to address emerging challenges such as climate change, nanotechnology, and endocrine-disrupting chemicals. Environmental justice should be a guiding principle in these efforts, to ensure that the costs of pollution and the benefits of environmental protection are shared equitably among all parts of society.

Ensuring Robust Scientific Input to EPA Decision Making
The EPA should review and strengthen the ways it uses the scientific expertise of its staff and advisory committees, especially in cases where scientific input is critical or the law requires it. The agency should also tighten its conflict-of-interest restrictions.

Disclosing and Mitigating Conflicts of Interest

The next EPA administrator should work with employees, industry, and the scientific community to develop comprehensive conflict-of-interest policies for both staff and members of advisory committees:

- Government employees and members of advisory committees who are involved in regulation should disclose all conflicts of interest and special interests that might affect their ability to do their job in an unbiased manner.

- Individuals with a significant conflict of interest may still contribute to a project as invited experts, but the EPA should restrict them from decision-making authority or otherwise influencing policy outcomes.

Conflict-of-interest policies should also prohibit the revolving-door practice of appointing individuals from industry as senior EPA officials who regulate those industries:

- The next administration should provide clear guidelines for minimizing the appointment of senior officials with conflicts of interest. At a minimum, federal employees should be required to recuse themselves from decisions involving former employers (RDWG 2005).

Reforming Advisory Committees

The EPA should pursue reforms to make better use of its independent advisory committees. Specifically, the next EPA administrator should work with the Clean Air Scientific Advisory Committee to improve the process for setting the National Ambient Air Quality Standards, to ensure that decision makers have access to the "best available science."

Depoliticizing Funding, Monitoring, and Enforcement
These actions are essential to restore the scientific integrity of EPA decision making. But, in addition, problems with funding, monitoring and enforcement—which relate to EPA's scientific integrity—also need to be addressed by Congress and the next President to ensure that the EPA is the robust environmental agency that our country needs. In particular, Congress should provide the EPA with resources commensurate with its growing responsibilities and should work to ensure that selective internal budget cuts are not used to punish inconvenient programs or

offices. The next president should commit to strong and consistent enforcement of the nation's environmental laws.

VI. Concluding Thoughts

The EPA's scientific enterprise is our nation's first line of defense against threats to public health and the environment. These threats are growing more complex and global, with the potential to harm the nation's health and prosperity. Despite notable successes, air and water pollution remain serious public health problems. Each year brings new and untested chemicals into our homes, schools, and workplaces. Climate change alone is projected to have profound impacts on public health, agriculture, the economy, and even national security.

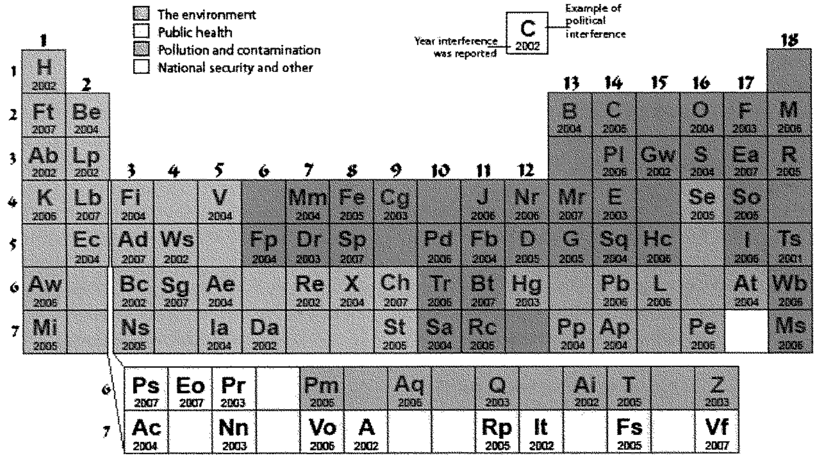
These problems are not insurmountable. The environmental and public health successes of the past several decades show that the country can rise to the challenge of environmental threats—but only if the EPA has the proper tools. Given the complexity of today's environmental challenges, a credible scientific knowledge base is essential to an effective response. To foster and sustain a healthy scientific enterprise, Congress and the next president should take concrete steps to protect EPA's scientists, make the agency more transparent, reform the regulatory process, strengthen the scientific advisory system, and depoliticize funding, monitoring, and enforcement.

Science is not the only element of effective policy making. However, because science enjoys widespread respect, appointed officials will always be tempted to manipulate or suppress scientific findings to support predetermined policies. Such manipulation is not only dishonest; it undermines the EPA's credibility and affects the health and safety of Americans.

The Bush administration's direct abuse of science—combined with systemic changes to the regulatory system that threaten the integrity of EPA science—highlight the need for strong action by the next president and Congress to restore scientific integrity to the agency's decision making. Only then can the EPA fully mobilize to serve the public good and ensure the nation's health.

A. The A to Z Guide to Political Interference in Science

In recent years, scientists who work for and advise the federal government have seen their work manipulated, suppressed, distorted, while agencies have systematically limited public and policy maker access to critical scientific information. To document this abuse, the Union of Concerned Scientists has created the A to Z Guide to Political Interference in Science. To read the full A to Z Guide visit http://www.ucsusa.org/AtoZ/.



From air pollution to Ground Zero, the *A to Z Guide* showcases dozens of examples of the misuse of science on issues like childhood lead poisoning, toxic mercury contamination, global warming, and endangered species. These 85 examples originate in 24 federal agencies and departments.

Timeline of abuses of science

April 2008	Integrity of EPA's toxics database threatened by interagency review
December 2007	All-terrain vehicle danger report
October 2007	NASA pilot survey Censoring climate change health hazards
August 2007	Mountain removal mining
July 2007	Surgeon general muzzled FEMA trailers
May 2007	Southwestern bald eagle Spotted owl
April 2007	Voter fraud
March 2007	Polar bear travel restrictions
February 2007	Lead testing of children's lunchboxes
January 2007	Executive Order 13422

December 2006	Lead national ambient air quality standards
October 2006	Prairie dogs
	Roundtail chub
	Tabernaemontana rotensis
August 2006	EPA closes its scientific libraries
	EPA ignores scientific studies on pesticides
July 2006	Education Department suppresses study on school vouchers
	NASA mission statement
June 2006	Changes in climate change websites
May 2006	STD Panel at CDC conference manipulated,
	Science disregarded for prescription drug Ketek
April 2006	National ambient air quality standards process changes
	Muzzled scientists at carbon conference
	Global warming news releases
	Minders on climate media interviews
February 2006	Navy downplays sonar impact on marine life
	Science suppressed on hurricane/global warming connection
	Bureau of Land Management suspends forest study funding
	EPA distorts evidence for tightening particulate matter standard
January 2006	NASA censors climate scientist James Hansen
November 2005	Economic analysis distorted for endangered red frog habitat
October 2005	EPA limits information about their release of toxic chemicals
August 2005	Department of Justice suppresses racial profiling study
July 2005	EPA report on fuel efficiency withheld
	Top FDA official overrules staff to approve nerve stimulator
June 2005	Bureau of Land Management altered a cattle grazing impact study
	Distortion and censorship of global warming documents
May 2005	Genetics eliminated from Endangered Species Act decisions
April 2005	World Health Organization approval of abortion pill block attempt
March 2005	New selenium pollution control standards misrepresent science
February 2005	First UCS surveys of federal agencies scientists released
December 2004	Endangered Species Act scientific documents altered for greater sage grouse
	Federally funded abstinence-only curriculum contains false science
November 2004	FDA ignores scientists' warnings on arthritis drug Vioxx
October 2004	EPA promotes flawed study on hydraulic fracturing, an oil drilling technique
September 2004	Endangered Species Act science ignored for the marbled murrelet
August 2004	Science obscured on health impacts of weedkiller Atrazine
	Forest Service exaggerates wildfire threat to spotted owl to promote logging
June 2004	Health Organization panel experts are vetted by Health and Human Services
May 2004	EPA uses bad science to create plywood plant pollution rule
	FDA appointees distort science to deny access to emergency contraception
	Research at the U.S. Fish and Wildlife Service is distorted
April 2004	EPA distorts guidelines for monitoring air pollution over national parks
	CDC researchers kept from international AIDS conference
	Fish and Wildlife Service distorted economic analysis of bull trout habitat
	NIH advisory board rejects scientists subjected to political litmus tests
March 2004	Science-based recommendations removed from an official report on salmon
	Scientists dismissed from President's Council on Bioethics
	Carbon sequestration pamphlet
February 2004	Arms Control Advisory Panel dismissed and never reappointed.
January 2004	Multiple agencies disregard science on mountaintop removal mining

December 2003	Office of Management and Budget adopts flawed peer review rule
	Administration officials manipulate Endangered Species Act science
August 2003	White House orders misleading of public on Manhattan air quality after 9/11
July 2003	National Nuclear Security Administration Panel dismissed
	EPA withheld an analysis of alternatives to President Bush's Clear Skies Act
June 2003	Administration officials undermined science behind climate change
March 2003	Forest Service overruled science-based old-growth forest management plan
February 2003	White House suppressed information on impact of mercury on public health
December 2002	Obscured scientific evaluation of abstinence-only education programs
	CDC ordered to change website about the effectiveness of condoms
	NIH Drug Abuse Advisory Panel subject to political litmus tests
	Abortion and breast cancer linked on National Cancer Institute website
	Microbiologist prohibited from publishing on airborne bacteria
November 2002	Workplace Safety Panel scientists rejected because of their beliefs
October 2002	Childhood lead poisoning panelists replaced by scientists with industry funding
	Underqualified doctor nominated to chair FDA reproductive health committee
September 2002	Administration disregarded scientific analysis of aluminum tubes in Iraq
	Engineer rejected from Army Science Board because of political contributions
May 2002	Manipulation of global warming science
August 2001	Fish and Wildlife Service misrepresented information on rare trumpeter swans

B. Selected Quotes from EPA Scientists Arranged by Topic

The following are selected quotes from EPA scientists who responded to a survey by the Union of Concerned Scientists. For more information about the survey, including the text of all essay responses, please visit http://www.ucsusa.org/EPAscience. The quotes are organized by topic.

When asked how to improve scientific integrity at the EPA, scientists said:

Political interference

There are still good scientists producing good science at USEPA. The main problem I see is an administration that considers science only if it supports its agenda. As in other areas, science is used only if it furthers preexisting policy; otherwise it is ignored, marginalized or suppressed (e.g. climate change).
-A scientist from the EPA regional offices

EPA needs dynamic, scientific leadership interested in the well being of the environment and public health. EPA should not be the political agency it has become, the right hand of industry and short economic gain.
-A scientist from the Office of Solid Waste and Emergency Response

Do not trust the Environmental Protection Agency to protect your environment. Ask questions. Be aware of political and economic motives. Become politically active. Elect officials with motives to protect the environment and hold them accountable.
-A scientist from the EPA regional offices

Political considerations should not trump environmental stewardship, and the EPA should not be forced to be silent on the environmental consequences of policy shifts.
-A scientist from the EPA regional offices

Do not allow other entities such as [the White House Office of Management and Budget] to interfere with, or suppress the publication of, EPA's scientific work products. Maintain an open peer review process.... Strengthen whistleblower protections for civil servants.
-A scientist from the EPA regional offices

EPA needs to be an independent agency and the amount of political interference needs to be curtailed.
-A scientist from the EPA regional offices

Keep political appointees from interfering in scientific decisions or publications. Do not allow political appointees to pressure authors to withdraw from publication or pressure their supervisors to carry out actions that inhibit publication.
-A scientist from the EPA regional offices

Funding and Staffing

MORE FUNDING! We do NOT have the resources to meet our mission. My division has seen its resources - in purchasing power- cut over 50% since 10 years ago.
-A scientist from the Office of Research and Development

EPA was created and began recruiting scientists in the 1970s; many have retired or will shortly do so. The inability to fill technical vacancies along with the loss of EPA libraries are bleeding down the EPA's technical knowledge base and our ability to provide or share the skills and knowledge that are critical to overall mission success.
-A scientist from the EPA regional offices

Increase the morale of the employees by providing incentives for growth. New hires, at least among scientists in my area are few and far between (no hires in almost 10 years) and the shrinking and aging employee population is more looking forward to retirement than providing ideas that work and will make a difference, because nobody seems to really listen.
-A scientist from the Office of Prevention, Pesticides, and Toxic Substances

External Interference

[The White House Office of Management and Budget] and the White House have, in some cases, compromised the integrity of EPA rules and policies; their influence, largely hidden from the public and driven by industry lobbying, has decreased the stringency of proposed regulations for non-scientific, political reasons. Because the real reasons can't be stated, the regulations contain a scientific rationale with little or no merit.
-A scientist from the EPA regional offices

Currently, [the White House Office of Management and Budget] is allowed to force or make changes as they want, and [EPA actions] are held hostage until this happens.
OMB's power needs to be checked as time after time they weaken rulemakings and policy decisions to favor industry.
-A scientist from the Office of Air and Radiation

External scientific advisory processes associated with risk assessment should not incorporate industrial perspectives. In other words, "risk management" should be recognized as a human values problem, and should be more explicitly separated from risk assessment.
-A scientist from the EPA regional offices

Openness

Remove the political screening step in science at the Agency. For example, we are not allowed to talk to the press when they call but must refer them to a person in the front office. Often this results in the press not getting the true facts but only those that don't make the Agency look bad.
- A scientist from the Office of Prevention, Pesticides and Toxic Substances

The premise should be that all documents (except enforcement related stuff) start out as public documents unless EPA has jumped through a lot of legal hoops to be able retain them.
-A scientist from the EPA regional offices

The science and risks and benefits need to be honestly and fairly considered. The decisions that are made should be justified and be transparent as to why a decision was made and the risks and benefits be clearly and honestly presented.
-A scientist from the Office of Prevention, Pesticides, and Toxic Substances

I perceive that there is a gag rule that prevents government employees from being allowed to tell the public what they have learned on the job, as well as their job-informed and educated opinions. This work, and knowledge gained during that work, is paid for by the taxpayers.
-A scientist from the Office of Air and Radiation

Scientific Review

Do not allow political appointees into the process of scientific review. Their job is to make management decisions, not influence the data and information before it is collected and presented.
-A scientist from the EPA regional offices

Improve the peer review process by not making it so cumbersome and by allowing those with real experience to participate.
-A scientist from the Office of Solid Waste and Emergency Response

One of the best current safeguards is review of Agency documents and policies by independent advisory boards including the Science Advisory Board, the Clean Air Scientific Advisory Committee, and the Board of Scientific Counselors. Much EPA work in human health risk assessment is now subjected to Inter-Agency Review by other Federal entities which appear to be more closely aligned with private interests than with the public health community.... Maybe more Congressional oversight would help the Executive Branch straighten its priorities.
-A scientist from the Office of Research and Development

Organizational Improvements

I have never seen morale at a lower point than we currently have in EPA. Good scientists are leaving because they can no longer put up with all the micro-management that is heaped on them in lieu of effective administrative leadership.
-A scientist from the Office of Research and Development

Reduce the power of [the White House Office of Management and Budget] over EPA scientific products. All communications between EPA and OMB during the development of Agency technical products and actions should be preserved for the public record.... In particular, implementation of OMB's risk assessment guidelines would be disastrous.
-A scientist from the Office of Air and Radiation

Make sure that there is no way that you can change the science to accommodate a political "need." Currently I think EPA's credibility is in the tank due almost entirely to trying to make the science fit a political need rather than openly admitting that both paradigms exist and then deal with the realities of both politics and science to make the decision.
-A scientist from the EPA regional offices

This is a young and small agency that has, since its inception, been under enormous pressures. The ability to protect the environment is often also bound by the laws that govern the agency. So, the best way to improve the scientific work at EPA is to ensure that appropriate governing laws are enacted so that with reasonable interpretation the goals of protecting the environment may be met.
-A scientist from the Office of Prevention, Pesticides, and Toxic Substances

EPA is by mandate a regulatory agency charged with protecting human health and the environment. To restore the integrity of scientific work at EPA, political appointees must be removed from all levels within the Agency. Those appointees influence ranges from subtle to direct manipulation of statutory/regulatory actions. Further, the influence of other agencies, particularly [the White House Office of Management and Budget] significantly affects the actions of specific individual program offices, which amounts to direct oversight of almost everything EPA does. These influences are not limited to manipulation of the results of basic scientific work, but from everything from how vigorously the Agency pursues oversight, weakening guidance and enforcement of statutes/regulations that are detrimental to human health and the environment.
-A scientist from the EPA regional offices

Respect for Science

My opinion of EPA has changed since being here. Specifically, I had believed EPA was more scientific in its approach. Now I realize that EPA has politically driven agendas that sometimes, not always, affects decisions of scientific nature.
-A scientist from the EPA regional offices

Science and technical information needs to be given more weight in decision-making rather than just seen as background information.
-A scientist from the EPA regional offices

Managers need to learn to trust the expertise of the technical staff.
- A scientist from the Office of Water

Take the politics out of science. Senior EPA leaders and White House officials over the past 6 years have used "junk" science along with biased opinions to make bad environmental decisions. EPA needs to be fully funded to perform its mission.
-A scientist from EPA headquarters

[The integrity of EPA science could best be improved] by allowing scientists with internationally acknowledged expertise to work and publish in their fields, instead of withholding support and restricting activity.
-A scientist from the Office of Air and Radiation

[The integrity of EPA science could best be improved] by staying true to the pollution laws that congress gives us (which means much more frequent revision to reflect the latest science), by leaving less discretion to the executive branch, and by giving the scientific advisory boards more weight to make decisions.
-A scientist from the EPA regional offices

Allow the science to drive policy rather than the other way around.
-A scientist from the Office of Research and Development

Other

Strong, independent oversight and protection of "whistleblowers" (real protection - not what is there now) could stem the most damaging practices.
-A scientist from the Office of Research and Development

As a user rather than producer of technical and scientific information, I find it very frustrating that I have to search out myself research findings and recommendations [of various advisory bodies] that directly affect the management of my programs. By the time the reports filter down to the staff program levels, they have either mutated beyond recognition during intervening manager reviews, or have simply been lost in the fog of the bureaucracy.
-A scientist from the EPA regional offices

1) Improve transparency in government by requiring comments from [the White House Office of Management and Budget] and other agencies on science documents to be made public
2) ensure science decisions on conclusions contained in EPA science documents are made by EPA career scientists
3) require political appointees to post summary of discussion (including any documents provided) and attendees when they meet with external stakeholders
4) encourage accountability in EPA political appointees through Congressional inquiry regarding basis for decisions and role of science versus political considerations in decision making
-A scientist from the Office of Research and Development

"[Restore] the Agency's public role as a faithful advocate for and protector of the environment, as opposed to publicly downplaying the need for action in so many instances. Such a stance would communicate from the top that we are all about scientific excellence because, at heart, we sincerely care about environmental protection."
-A scientist from the Office of Research & Development

C. Scientific Freedom and the Public Good

On February 14, 2008, a group of prominent scientists called on the U.S. government to establish conditions that would enable federal scientists to produce the scientific knowledge that is needed by a government dedicated to the public good.[27] *In an accompanying report,* Federal Science and the Public Good,[28] *UCS details specific steps that Congress and the administration can take to restore scientific integrity to federal policy making.*

Scientific knowledge and its successful applications have played a large role in making the United States of America a powerful nation and its citizens increasingly prosperous and healthy. The challenges that face the United States in the twenty-first century can only be met if this tradition is honored and sustained.

To that end, the U.S. government must adhere to high standards of scientific integrity in forming and implementing its policies. Breaches of this principle have damaged the public good and the international leadership of the United States. To meet its obligation to serve the public interest, the government must have reliable scientific work and advice at its disposal, and provide the public with reliable scientific information. This requires the government to provide federal scientists with the resources and the professional environment necessary to carry out their missions effectively and honestly. The government should also draw on the knowledge of federal scientists and of the larger scientific community to formulate public policy in an objective and transparent manner.

Scientists employed by government institutions commit themselves to serve the public good free from undisclosed conflicts of interest and to carry out science that is reliable and useful, while respecting statutory limitations such as national security laws. Therefore, government scientists should, without fear of reprisal or retaliation, have the freedom:

- to conduct their work without political or private-sector interference;
- to candidly communicate their findings to Congress, the public, and their scientific peers;
- to publish their work and to participate fully in the scientific community;
- to disclose misrepresentation, censorship, and other abuses of science; and
- to have their technical work evaluated by scientific peers.

We call on Congress and the executive branch to codify these freedoms, to establish stronger means for gathering scientific advice, and to take concrete steps to enhance transparency, so as to create conditions conducive to a thriving scientific enterprise that will serve our democracy with integrity and bring the full fruits of science to all Americans and to the world.

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[27] For more information and to see the names of the endorsers go to http://www.ucsusa.org/scientific_integrity/restoring/scientificfreedom.html.

[28] To read the text of the report go to http://www.ucsusa.org/scientific_integrity/restoring/federal-science.html.

D. Previous UCS Surveys of Federal Agency Scientists

Previous UCS surveys have given voice to over 1,800 scientists across the federal government. Full results for these surveys can be found at http://www.ucsusa.org/surveys/. The survey findings include the following:

U.S. Fish and Wildlife Service (FWS)
In February 2005, the Union of Concerned Scientists (UCS) and Public Employees for Environmental Responsibility (PEER) released the results from a 42-question survey distributed to 1,410 FWS biologists, ecologists, botanists and other science professionals working in Ecological Services field offices across the country. The survey was designed to obtain their perceptions of scientific integrity within the FWS, as well as political interference, resources and morale. 414 scientists returned completed surveys (29 percent), despite agency directives not to reply—even on personal time.

Notable results include:

- Nearly half of all respondents whose work is related to endangered species scientific findings (44%) reported that they "have been directed, for non-scientific reasons, to refrain from making jeopardy or other findings that are protective of species."
- One in five agency scientists revealed they have been instructed to compromise their scientific integrity—reporting that they have been "directed to inappropriately exclude or alter technical information from a FWS scientific document," such as a biological opinion.
- More than half of all respondents (56%) knew of cases where "commercial interests have inappropriately induced the reversal or withdrawal of scientific conclusions or decisions through political intervention."

National Oceanic and Atmospheric Administration (NOAA) Fisheries
In June 2005, UCS and PEER released the results from a 34-question survey distributed to 464 NOAA Fisheries biologists, ecologists, botanists and other science professionals working in headquarters and regional and field offices across the country. The survey was designed to obtain their perceptions of scientific integrity within the agency, as well as political interference, resources and morale. 124 scientists returned completed surveys (27 percent).

Notable results include:

- More than one third of respondents positioned to make such recommendations (37%) have "been directed, for non-scientific reasons, to refrain from making findings that are protective" of marine life.
- Nearly one in four (24%) of those conducting such work reported being "directed to inappropriately exclude or alter technical information from a NOAA Fisheries scientific document."
- More than half of all respondents (53%) knew of cases where "commercial interests have inappropriately induced the reversal or withdrawal of scientific conclusions or decisions through political intervention."

Food and Drug Administration (FDA)

In June 2006, UCS and PEER released the results of a 38-question survey distributed to 5,918 scientists at the FDA to obtain their perceptions about scientific integrity. 997 scientists filled out and returned the survey (17 percent).[29]

Notable results include:

- Almost one in five (18 percent) responded, "I have been asked, for non-scientific reasons, to inappropriately exclude or alter technical information or my conclusions in an FDA scientific document."
- Three in five (60 percent) knew of cases "where commercial interests have inappropriately induced or attempted to induce the reversal, withdrawal or modification of FDA determinations or actions."
- Approximately half of the respondents (51 percent) felt the "FDA is acting effectively to protect public health."

Federal Climate Scientists

In January 2007, UCS released the results of a 40-question survey distributed to 1,630 climate scientists at seven federal agencies (NASA, NOAA, EPA, USGS, USDA, DOE and DOD) and 119 climate scientists at the independent National Center for Atmospheric Research (NCAR). 279 federal scientists and 29 NCAR scientists filled out and returned the survey. The survey results were released as a joint report with the Government Accountability Project (GAP) entitled *Atmosphere of Pressure.*[30]

Notable results include:

- 150 scientists (58 percent) said they had personally experienced at least one incident of political interference in the past five years.
- Nearly half of all respondents (46 percent) perceived or personally experienced pressure to eliminate the words "climate change", "global warming" or other similar terms from a variety of communications.
- More than half of respondents (52 percent) said that their agencies always or frequently require public affairs officials to monitor scientists' communications with the media.

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[29] For more information about the FDA survey go to http://www.ucsusa.org/scientific_integrity/interference/fda-scientists-survey-summary.html.

[30] To read the text of the report go to http://www.ucsusa.org/scientific_integrity/interference/atmosphere-of-pressure.html.

Mr. STUPAK. Thank you, and thank you both. We will go to questions, and I think we are going to go 10 minutes and give everybody an opportunity so we can move the panels right along.

You both mentioned transparency, the need for transparency in the deliberations and in reports and studies that the EPA does, but Dr. Grifo, let me ask you because you have done this survey, and your survey shows that political interference with science has increased over the past several years. What do you think are the consequences of inaction, if nothing happens—you gave us three recommendations, if the Congress did nothing—from your point of view, on behalf of the scientists?

Ms. GRIFO. From my point of view, I think one of the scariest things that is going on or come out of my conversations independent of this survey were conversations that I have with young scientists at the EPA, scientists who say to me, we are waiting, we are staying until January, February to see what happens, but after that, we are leaving because there is no place in this agency for innovation and for a young scientist to really blossom and grow. And to me, that is frightening. We are at a point anyway with the EPA where retirements are happening because of the date that the Agency was founded. Many of its scientists are at retirement age, and if we don't have a young crop of scientists who are enthusiastically there, I think that is a huge problem, but obviously there are many other consequences.

Mr. STUPAK. In your report, you mentioned, I think, about 500 scientists responded. One hundred mentioned the OMB as being sort of a source of interference here. Can you give me some examples of some of those comments? What did they mean, like source of interference? What did they allude OMB does, Office of Management and Budget?

Ms. GRIFO. There were a number of things, and I want to be clear that we did not ask them about OMB. We asked them how could political interference at the EPA, or how could scientific integrity be restored at the Environmental Protection Agency, and as you said, nearly 100 scientists came back and said, you know, it is about OMB. Some of the specific quotes: "Restrain the Office of Management and Budget. This administration has not only watered down important rules protecting public health, they have also altered internal procedures so that scientific findings are accorded less weight." Another one: "In this administration, self-censorship is almost as powerful as the political censorship. Options that OMB or the White House wouldn't like aren't even put forward," and I think that is another serious issue. I think if the line is unclear in terms of what you can say or do, you don't even want to come near that line and so we find scientists not even approaching a study that they think could potentially be controversial, and so on. There are many, many comments and they are all on our Web site.

Mr. STUPAK. Thank you.

Mr. Stephenson, if I may, I said that you had mentioned transparency in your testimony, and why is transparency important in this process?

Mr. STEPHENSON. Well, as I mentioned, it is a principle of sound science, and even the appearance of a conflict of interest is a problem, and what EPA has been doing lately is mixing the science part of risk assessment with the management and policy part. The science is the science. I can imagine a situation where an agency would have a piece of research that should be held deliberative. The science is the science so the facts drive that. So if they want deliberative comments in the policy or the policymaking part of this, that may be OK, although I think the entire agency should be transparent.

Mr. STUPAK. So is it fair to say the policy is spilling over into the science part of it as to whether—like TCE, you mentioned TCE in your testimony—or not that should be listed as a cancer-causing agent. The science is one thing, policy is another thing, how you handle it. They should be independent of each other, should they not?

Mr. STEPHENSON. Right, and you have to do reassessments at least every 10 years on all the 500 chemicals that are in there, so if you are constantly reevaluating or holding until additional research is done, there is lots of problems beyond just transparency just in the length and the cumbersomeness of the process itself. We have to get this done quicker.

Mr. STUPAK. Well, the reason why I mentioned TCE, this subcommittee has held a number of hearings on TCE at Camp Lejeune which has gone way, way back many, many years and we are still trying to get some kind of IRIS completed on TCE so we can begin the process and the policy decisions can take place and different administrations are going to disagree how you handle it, but how do we move past that? How do you get TCE on the IRIS? It has taken how long? Eight years? And is it completed yet?

Mr. STEPHENSON. Ten plus. That is just one example that we used. We offer several specific recommendations in our report to handle this, for example, giving advance notice when an assessment is going to begin so that the research can be done prior to the assessment actually starting. Don't hold up a risk assessment like TCE for 2 years waiting for the National Academy to come up with additional information and then that information simply confirms what EPA has already done. Do that before that. The IRIS is supposed to capitalize on existing scientific research. It is not doing anything new. Why does that process take 10 years to assemble the best available science on a given chemical?

Mr. STUPAK. Well, if EPA had already made its decision and required the National Academy of Science to look at it, they reaffirm what EPA did, then why don't we have TCE out there as on the IRIS and here is the risk associated with it?

Mr. STEPHENSON. That is a very good question. I can't explain that.

Mr. STUPAK. Do you know of any scientific information that would prevent that from happening?

Mr. STEPHENSON. We are not a science organization but we can read the research and we can read the science. What we are suggesting, there needs to be more organization in this process. TCE was done under the old process before comments were declared deliberative and it took that long in the old process. Now there are several new steps that have been introduced into the new process like the two new OMB reviews. OMB contends that EPA owns the process. All throughout our investigation they said EPA owns this process yet if you look at the OIRA part of OMB, they recognize that EPA loses control of the process once the assessment goes to OMB, so it is a left hand-right hand syndrome at OMB.

Mr. STUPAK. So why is OMB's process in the dark? Why is that not open to transparency?

Mr. STEPHENSON. Well, it is not OMB. OMB is trying to facilitate and coordinate interagency comments, from DOD, from the Department of Energy, but why that shouldn't be done in the open for a scientific process like a risk assessment, we can't explain.

Mr. STUPAK. Well, in this flow chart—and Kyle, if you can bring up the flow chart. Bring up the one, the current one, post April 10, 2008.

[Chart shown.]

Mr. STUPAK. And the reason why I bring that one up, it is pretty wild, but not only is it hard to follow, but it looks like it is open to review until we get to the OMB part, then we go into sort of like secret and then it pops back out and there is some more review and then we go back into OMB again, we are secret, then we get right back to OMB one more time, the final process. Why is this process open, closed, open, closed throughout this? Any justification for it?

Mr. STEPHENSON. From an interagency comment point, it is closed until the assessment becomes final and then it is provided to the general public, it is peer reviewed, but no one, no scientist, the general public, nobody knows what kind of input that the Department of Defense or the Department of Energy or OMB for that matter might have had. We don't—nobody knows. The point is, the public has to have confidence that this scientific assessment is done in the sunlight, and this particular process doesn't support that objective.

Mr. STUPAK. And this process probably doesn't show it. Is it safe to say, does EPA even own this process anymore? Is it basically OMB that controls this process?

Mr. STEPHENSON. Well, it depends upon which part of OMB you ask, but the management part will say that EPA owns the process but when you look at the part reviews, the OIRA part of OMB admits in the part reviews that EPA loses control of that process once the assessments are submitted to OMB.

Mr. STUPAK. EPA is always going to say they control the process because it is supposed to be their process but from the testimony and studies I am seeing, OMB looks like they control it. So you as a member of Government Accountability Office, what is your assessment? Who owns this process? Who is controlling this process, EPA or OMB?

Mr. STEPHENSON. We couldn't get past asking OMB the question. OMB says EPA owns it. It appears to us that OMB owns the process at a certain phase.

Mr. STUPAK. So it would appear that OMB owns the process?

Mr. STEPHENSON. EPA can't move forward on a risk assessment until it gets clearance from OMB, until the interagency reviews are complete, so——

Mr. STUPAK. OMB coming into this process, this is just—has this occurred under this Administration or has it happened under other Administrations?

Mr. STEPHENSON. OMB has always coordinated interagency comments on anything. That is one of their functions. That is part of the M in OMB, the management function to facilitate the federal family of agencies. However, it should be done in this case from a scientific process in the sunlight. That is our big concern with this.

Mr. STUPAK. Kyle, go back to Number 1, the first one of this, the pre-2004.

[Chart shown.]

Mr. STUPAK. This is the pre-2004. I don't really see much where OMB is in that process. They don't have a designated spot in there, do they, where they would come into this process other than overall coordination?

Mr. STEPHENSON. No.

Mr. STUPAK. OK. Then Kyle, go to the second one, and this is from 2004 to 2008.

[Chart shown.]

Mr. STUPAK. I see OMB in there two places, Number 9 on the top there and then Number 13 in the lower right-hand corner where final OMB interagency review and approval, and then Kyle, go to the last one. I see OMB, and I am just doing a quick look here, about three times in it, Number 9 again, Numbers 12A and 12E, and one place earlier too, I guess that would be pretty close to four of them. But it just seems like this process gets more bogged down. Have the chemicals being looked at, have they been—has the process greatly slowed down under this new schematic?

Mr. STEPHENSON. It has only been in force since April.

Mr. STUPAK. It is hard to say then, I guess.

Mr. STEPHENSON. What we are suggesting is if DOD thinks that the research or the scientific evidence isn't sound on a given chemical, it can request additional studies like it did on TCE of the National Academies. National Academies is a busy place. It took them 2 years to complete their assessment, which reaffirmed what EPA had already said when it amassed the scientific evidence on TCE at the time. So this constantly repetitive sending it back to OMB, do more research, look at the sensitivity analysis, do more research, it just never gets out of this process and it is supposed to assimilate existing scientific research. It is not supposed to be creating new research on a given chemical. How can that process take 10 years?

Mr. STUPAK. My time is up. Mr. Shimkus for questions, please.

Mr. SHIMKUS. Thank you. I want to ask Ranking Member Barton, do you still want to—all right.

Kyle, if you would put the messy one up.

[Chart shown.]

Mr. SHIMKUS. No one is going to try to defend this process, no one, so that is just bureaucratic slowing down the processes and it is not efficient and you will find no one on our side trying to defend that, and that definitely has to be streamlined.

Dr. Grifo, who funds the Union of Concerned Scientists?

Ms. GRIFO. We are funded by our membership and by foundations.

Mr. SHIMKUS. And can you name the foundations?

Ms. GRIFO. Not all of them. They are in our annual report on the Web site but I can name the ones, a couple—Hewlett Foundation, Packard Foundation, it is a long list.

Mr. SHIMKUS. Can you tell me how this report that you published was peer reviewed, and was it done as we expect the EPA to do it publicly and externally?

Ms. GRIFO. Yes.

Mr. SHIMKUS. And can you tell me who peer reviewed it?

Ms. GRIFO. Yes, it is on the acknowledgements page, roman numeral VII. It is listed David Michaels, Mike Walsh, Eric Shaffer, Molly Churchill, Rick Melburth, Michael Halpern, Kathy Rest, Kurt Gottfried, and an unnamed former EPA scientist providing valuable comments. We also had a steering committee early on in the process as well.

Mr. SHIMKUS. Obviously I am going to base most of my questions on the CRS report because my frustration is, you want it both ways. I think because you knew we had the CRS report, then you had a chance to respond in writing, which is in the binder, but at one point you say it was a census but then in your testimony in the questions you say, well, we are going to extrapolate this to the whole body. You really can't have it both ways. Either it is a census or it is a credible poll that you can extrapolate to the whole body, and for scientists to claim support of the scientific method and not use a scientific process is frustrating. Some examples, on page 2 of the report, the CRS report states that what constitutes such interference as opposed to editorial differences and policy or substantive disagreements is not spelled out for the respondents. One person's political interference might be another's heavy-handed editing. The report gives us examples of political interference. Aside from that, how do you define it?

Ms. GRIFO. It is actually defined in the questionnaire that the scientists had.

Mr. SHIMKUS. Well, I am asking, how do you define it?

Ms. GRIFO. Well, I can refer you to that page in the report where it specifically lists a specific—it is on page 73 of the report and it is a very long list of about 10 different things, and this is the list that was given to the scientists when they were given this to respond to.

Mr. SHIMKUS. How do you answer the concern that the way you phrase questions about political interference may have in fact influenced the way people answered these questions?

Ms. GRIFO. We used political interference twice at the very end of the survey and where we used it was just above this list where we defined it. I would also like to say, I think there is another misconception which is that the entire report and the conclusions are based on the survey. They are not. The report is comprised of both qualitative and quantitative information. I think when we look at the list of incidents, we interviewed and——

Mr. SHIMKUS. Let me reclaim my time and stay on this political interference discussion. Your report in defining political interference gave a number of examples of situations that could construe to political interference. These include directed to exclude or alter technical information in report, changes or edits during review that change the meaning of scientific findings. Is it possible that some of these situations may be the result of good-faith disputes about science rather than the product of interference?

Ms. GRIFO. I think if we look at the long list of incidents that we have documented at the EPA, I think we would be hard pressed to call them heavy-handed editing. I think if we look at, you know, the mercury in power plants, new source review, OMB and the EPA——

Mr. SHIMKUS. You know, I can debate——

Ms. GRIFO. There is a long list of documents.

Mr. SHIMKUS [continuing]. New source review from the electricity generation debate which has a false premise that when you replace a more efficient generator, that you have to redo the whole EPA permitting when you get a bigger, higher input versus that. So I mean, we can talk new source review all we would like but——

Ms. GRIFO. Could we go to page——

Mr. SHIMKUS. No, ma'am, it is my time. We deal with surveys and polls all the time. Here is a summary. Terms and phrases used in the questionnaire are vague. A control group was not included. Longitudinal analysis was not conducted, which means this environment of corporate culture at the EPA may have existed in previous administrations but since you did not do a longitudinal analysis, you make a political attack on this Administration based upon an unscientific poll. Some questions—and this is just from the CRS report. This is not me. Some questions relied on what the respondent knew of or hearsay.

Ms. GRIFO. That was to get at the culture at the Agency. That was not to document incidences.

Mr. SHIMKUS. Hearsay.

Ms. GRIFO. In agencies like this, culture is very important.

Mr. SHIMKUS. Hearsay, a scientist using hearsay to attack the scientific process of the EPA. I just find that members of Congress, if we would use hearsay, we would get held accountable.

Ms. GRIFO. We did not draw our conclusions based on hearsay. The hearsay was there to measure the culture——

Mr. SHIMKUS. OK, let us go to another one. The respondents likely included those beyond the intended sample such as non-scientists and was biased toward senior scientists. The sample was not designed so that results can be extrapolated to a total population.

Ms. GRIFO. Yes. Correct.

Mr. SHIMKUS. But your statement, in your opening statement, you talk about, you making it widespread abuse. If you are going to say widespread abuse, what are you saying? We are going to extrapolate that. So that is why you can't have it both ways.

Ms. GRIFO. Could I respond?

Mr. SHIMKUS. If it is a census, then you can't say widespread. If it is a poll that has a sample size and it has been done randomly, we all know that, how polls operate, then you could extrapolate for the whole body. But you can't have, you just can't have it both ways. And I think the frustration point here is again scientists attacking the Administration and the EPA using an unscientific poll. The original questionnaire and data limitations are not included in the analysis. The conclusions drawn from the analysis may be inappropriate instances in which no opinion responses to a question exceed 20 percent. And then the results of these investigations show an agency under siege from political pressures, that is your comment, on a number of issues ranging from mercury pollution to groundwater, which you have mentioned, to climate change, political appointees, the Administration have edited—and here is a response to that statement. However, depending upon the population base used, the percentage who personally experienced at least one incident of political interference is either 56 percent or 15.3 percent, which may influence one's perception of whether the EPA is under siege. Fifty-six percent, oh, we got a problem. Fifteen percent, who knows. Maybe disgruntled individuals.

Ms. GRIFO. Eight hundred and——

Mr. SHIMKUS. In addition, the survey respondents were not asked questions about specific environmental issues such as those in the quote mercury pollution. This is not my report, ma'am.

Ms. GRIFO. Well, if I could——

Mr. SHIMKUS. This is a congressional resource.

Ms. GRIFO. You know, later on in the——

Mr. SHIMKUS. Ma'am, it is my time. So it is unknown as to which environmental issues survey respondents were referring to when they indicated political interference had taken place. That is my frustration. Now you have time, ma'am.

Ms. GRIFO. Thank you. Also in the CRS report, they acknowledge that they didn't have all the materials that they needed in order to do this analysis. This report was not done in any sort of consultation with us where we could have provided them with the screens that the scientists saw when they took the survey. They didn't have that information. They didn't have information, other parts of our research methodology.

Mr. SHIMKUS. Can I ask a question?

Ms. GRIFO. And CRS—could I finish? I think this is my time.

Mr. SHIMKUS. No, it is not. Ma'am, it is not your time.

Mr. STUPAK. It is technically Mr. Shimkus's time.

Mr. SHIMKUS. Let me ask why didn't you just do a survey, a scientific survey with a random sample to be able to extrapolate to the whole?

Ms. GRIFO. Because of the lack of transparency at the Agency. We did not have access to a full list of the scientists at the Agency. We had to construct that ourselves. We did not have the cooperation of the Agency.

Mr. SHIMKUS. Did you ask?

Ms. GRIFO. Absolutely we asked.

Mr. SHIMKUS. Was it in writing or by a phone call or an e-mail? Do you have documents that support that request?

Ms. GRIFO. We had conversations that we had trying to get that list.

Ms. SHIMKUS. Do you have a phone log?

Ms. GRIFO. I could probably find one.

Mr. SHIMKUS. That would be helpful to us. Science under siege, if you are going to use science to attack that science is under siege from the scientific community, I would request that you have scientific background to do that.

I yield back, Mr. Chairman.

Mr. STUPAK. Do you want to answer?

Ms. GRIFO. I would love to.

Mr. STUPAK. I will let you answer. It should also be noted just for the record, and I am sure Mr. Shimkus realized that their response to the CRS is found at tab number 29 in our binder. It is right there——

Mr. SHIMKUS. That is true, Mr. Chairman, and I think it would be fair for the Majority and for Dr. Grifo to appreciate the fact that we are the ones who found the CRS timely manner to the Majority so you had an opportunity to respond. It was because of what the Minority did to give you the opportunity to respond in writing.

Mr. STUPAK. It is there. It is exhibit number 30. We never move until the end of the hearing so without objection, tab number 29 in our hearing book will be part of the record. We will do it right now. If you care to respond, I will give you a minute.

Ms. GRIFO. Thank you.

Mr. STUPAK. Mr. Shimkus has the right to take all 10 minutes to ask a question if he wants, but you have time and then we will move on to Mr. Dingell.

Ms. GRIFO. Thank you. Many, many things that need to be clarified. First of all, the CRS report was sprung on us during testimony at a hearing in May. There was no notice whatsoever. The response was constructed after that hearing so this was not a gift from anyone. I think we can turn to the last paragraph, to the last page of the CRS report, and it says it is difficult, you know, to tell whether or not any of the critiques identified above would change the public's perception of the survey results regarding this issue. Further, it is important to keep in mind that for many in the science and engineering community, even one case of political interference would be considered to be improper. Independence is a critical part of this community's value system regardless of whether they are working for government, universities, or industry. In the response that we did, we go into a lot of the specifics but I think the key point is the conclusions that we made regarding those other issues and regarding the Agency as a whole are not based solely on the survey. They are based on qualitative research as well as that quantitative research. Both of them come together to produce those results. As I have said, there is a long list of examples: mercury in power plants; OMB in EPA; climate change. I hardly think that removing a reference to numerous studies such that EPA itself didn't even leave the chapter in a draft report in the environment in 2003, I think that is a lot more than heavy-handed editing that we are talking about here. And there are many examples: particulate matter; ozone, peer review, risk assessment, IRIS, program assessment tool rating; EPA and communication barriers; communication of climate change science; right to publish; particulate matter; and ozone, I have talked about—and on and on—lead, NOO_x, hydraulic fracturing, library closures. It is a very long list. I believe that we have a lot of evidence that supports our conclusion, and I would just end with the statement that 889 scientists reporting interference in the last 5 years, that is a number that is far too large to be acceptable, and at a hearing in May, Dr. Gray accepted that, that that number was too large. Thank you.

Mr. STUPAK. OK. That concludes the questions of Mr. Shimkus. Mr. Dingell is not back yet so we will go to Mr. Melancon for questions, please, 10 minutes.

Mr. MELANCON. Thank you, Mr. Chairman. I appreciate the opportunity. I was going to offer Ms. Grifo the opportunity to comment since the time for the other member had run out.

I guess one of the questions or one of the things that I have observed in one of my previous careers was scientists that feel that people are trying to direct their data to where they want it to go. Is that, do they actually do the science, do the report and then after the fact OMB and others are trying to delete or change or alter the outcome, Dr. Grifo?

Ms. GRIFO. Yes, I think one of the most startling examples of that does have to do with mercury and power plants. It has to do with the example where the clean air mercury rule. This took place in 2005. We have evidence that the White House and utility companies and power companies shaped this rule when in reality it should have been based on the science that was coming from the scientists at the EPA, and we have significant documentation to that effect that I am happy to share, and that is one example, you know, of many that we could bring up.

Mr. MELANCON. And Mr. Stephenson, from your perspective, the analogy that you can't have it both ways, do you feel that that in fact is the case or do you feel that the information that you were able to obtain and of course obviously not being able to follow the paper trail all the way through the process because it disappears at points in times, do you feel that there is validity? I have always been a believer if there is smoke, there is fire. Do you believe that from your review, from, I would assume your interviews with people within the Agency, that in fact there is interference?

Mr. STEPHENSON. We didn't try to ascribe blame or—what actually transpired. Our problem is with the process itself. No scientific process should be deliberative. You have just got to be more organized in these risk assessments than get them done quicker. We didn't try to say there was political influence or anything else. We just noted how many times OMB can stop the process at DOD's direction or anything else, ask for additional research, ask for uncertainty analysis, ask for a lot of things and continue to go back to the drawing boards on these assessments. They simply have to be done quicker than 10 years if they are going to be effective. We can't leave the public exposed to a dangerous chemical while we are waiting for them to complete a risk assessment.

Mr. MELANCON. So for either or both, where do we get someone to give us an objective diagram of how the process works so that we take manipulation either from the Congress or from any administration out of the process so that when we are delivered a report, we know that report has got all the scientific data right, draw your own conclusions if you would, but is there a place or an organization that can help us streamline, as Mr. Shimkus would like to do, which I agree with, and to make it so that when the data is there, we know that the data is in fact legitimate scientific data?

Mr. STEPHENSON. In our view, that is the importance of transparency for the science to be done in the sunlight so it would be huge to remove the black box. If the Department of Defense or Department of Energy or OMB or any other agency, for that matter, has a problem with the scientific assessments that EPA has done and has additional research to provide towards that science, it should be in the public. Why should that be done in a backroom?

Mr. MELANCON. I agree with you. I totally agree with you. The peer review process, and I think at some point in time they are talking about looking at what the science, and I think what happens, my experience has been, scientists just don't go in a cubicle all day long. They come out and they communicate with their counterparts what they are thinking, what they are hearing, what they are seeing, what they are feeling, because that is where they get the food for thought to go forward. Has there been a hindrance in that processing do you believe because of the concern with OMB or any other agency or even the Congress coming in and somebody—the fear of somebody looking over your shoulder and saying well, you are going in the wrong direction? I mean, is there a fear even working with your fellow scientists that maybe somebody would cause you problems?

Ms. GRIFO. In fact, we did ask a question in the survey about retaliation and fear of retaliation, and hundreds of scientists reported that but I think what is really telling is that 492 felt that they could not speak candidly within the Agency. This is not talking to the press, this is not talking to colleagues at universities. This is simply within the Agency, and 382 felt they could not do so outside the Agency, but setting the survey aside for a moment, there are also many other examples. If we look at the publication policies, the EPA peer review handbook, if we look at several scientists reporting problems with press contacts, if we look at, Dr. Titus, who was a project manager, was not—had interference in his desires to have an interview with the New York Times and so on and so forth. So we also have examples of scientists not being able to go to meetings. One colleague at a meeting went so far as to say if the scientist doesn't come, we are going to have 20 minutes of silence in the place where their talk would have been because they were so baffled by the fact that this scientist couldn't come. I think as you have rightly said, secrecy is an anathema to the scientific process. Scientists move ahead, the entire process moves ahead through this very transparent deliberative process, and that I think is a really frightening aspect of this closed-door deliberations, of these closed-door deliberations.

Mr. MELANCON. How many scientists do you have at the Agency?

Ms. GRIFO. We don't have a number. At the hearing in May, Dr. Gray, I think, said 7,000 scientists at the EPA.

Mr. MELANCON. That is a lot of scientists to be paranoid now.

Ms. GRIFO. Even one would be too many.

Mr. MELANCON. Yes, ma'am. Thank you.

I yield back my time.

Mr. STUPAK. Thank you, Mr. Melancon.

Mr. Barton for questions, please.

Mr. BARTON. Thank you, Mr. Chairman. I am going to focus most of my questions to Dr. Grifo.

I will just ask a general question to Mr. Stephenson because we have, one of the examples before us is the removal of Dr. Rice from a peer review panel on the chemical deca because she had stated to the Maine Legislature that she thought deca was a hazard, and if I understand correctly, should be banned, so they put her on this panel and then the industry complained that she was on the panel because she had announced, basically, a conclusion before the panel did its review. Mr. Stephenson, if you were accused of some crime and were on trial, would you want somebody on the jury who already had said publicly that you were guilty?

Mr. STEPHENSON. Of course not.

Mr. BARTON. So there may be a valid reason that Dr. Rice should have been on that panel but there also appears to be sufficient reason that she shouldn't have been.

Mr. STEPHENSON. Well, there are special rules. The peer review panels are large and balanced intentionally so——

Mr. BARTON. But you don't normally——

Mr. STEPHENSON. One peer reviewer should not theoretically make a difference.

Mr. BARTON. But you wouldn't put somebody on a peer review panel that already had a conclusion about the subject under consideration?

Mr. STEPHENSON. I don't know the situation but logically it doesn't seem like you would.

Mr. BARTON. OK. Let us go to Dr. Grifo. You say in your written testimony down at the bottom on your introduction, and I quote, "Our report documents changes in EPA policies regarding risk assessments that allow polluting federal agencies more control over the science." What is a polluting federal agency?

Ms. GRIFO. Well, I think in this instance, we were referring to the Department of Defense and the chemical that was already alluded to in the GAO report.

Mr. BARTON. So you are just stipulating that at least the Department of Defense is a polluting agency and you used the plural "agencies."

Ms. GRIFO. That is one. There are other instances. Department of Energy. I can provide you with full documentation of those instances.

Mr. BARTON. You just assert that these federal agencies are themselves polluters.

Ms. GRIFO. The federal agencies are responsible for chemicals that they are releasing in the course of their mission-driven duties and releasing a chemical that is potentially dangerous to public health into the environment, I think we would have to—that would be my definition.

Mr. BARTON. So you want us to eliminate or shut down the Department of Defense and——

Ms. GRIFO. No, I want——

Mr. BARTON [continuing]. Energy?

Ms. GRIFO. Sorry, sir. I didn't mean to interrupt. I think that there has been in the past a deliberative process that was more efficient and more transparent by which these things were resolved. No one is saying that OMB should not have a coordinating role. I think that is a very appropriate role for the Office——

Mr. BARTON. I didn't ask you about OMB yet. When you make the assertion that our federal agencies are themselves polluters, that does show to me somewhat of a bias, at least by yourself. I would hate to know what you think about the House of Representatives.

Ms. GRIFO. We are all polluters, sir. I will grant you that point. We are all certainly not perfect in that regard. But I do think that if an agency is using a chemical or putting a chemical into the environment that is potentially damaging to public health, then that is a cause for deliberation and concern and we need to have a process that respects that.

Mr. BARTON. I agree with the last statement. In the second page, you say, "The White House has rewritten EPA's scientific documents concerning climate change and pressured EPA scientists to support predetermined conclusions regarding mercury pollution." What predetermined conclusions did the White House pressure EPA scientists to adopt?

Ms. GRIFO. I don't think you have to take my word on that. EPA Inspector General Nicky Tinsley confirmed in February 2005 that EPA scientists were pressured to change their analysis——

Mr. BARTON. No, no, I want to know what the predetermined conclusion is.

Ms. GRIFO. Well, this particular example was about the level of mercury that was allowable under the clean air mercury rule.

Mr. BARTON. But the level, the parts per billion or parts per million, you are saying that the White House knew beforehand what the level should be and forced the EPA to put that level into the rule?

Ms. GRIFO. I am saying that the Inspector General——

Mr. BARTON. If you believe that, let us document it, OK? Don't just say it, let us document it. I don't think that statement can be substantiated but I don't know, but if you know, let us put that in the record. That is what the oversight subcommittee is all about.

Ms. GRIFO. We will be happy to.

Mr. BARTON. Now, later on on this same page you say, "Political interference has penetrated deeply into the culture and practices of federal agencies." Do you believe a president of either political party should not have the right to put his or her political appointees at the top of these federal agencies?

Ms. GRIFO. No, sir, I believe that is entirely appropriate.

Mr. BARTON. If it is appropriate, and I agree with you on that, should not these political appointees have some ability to oversee and influence the culture and practice of the federal agency that they are the appointee to?

Ms. GRIFO. They should not have the ability to change the science, to manipulate science——

Mr. BARTON. That is not my question.

Ms. GRIFO. And I don't think they should have the ability to intimidate the scientists.

Mr. BARTON. You said that——

Ms. GRIFO. That is part of the culture, I would say.

Mr. BARTON [continuing]. Political interference has penetrated deeply into the culture and practices of a federal agency, and I don't know how many federal employees we have on the Administration side but it is tens of thousands, maybe hundreds of thousands. We have got, I think, 500 presidential appointees. Now, I could be wrong on that, and Mr. Stupak or you can show me, but it is——

Ms. GRIFO. Close enough.

Mr. BARTON [continuing]. A small number. Those individuals, whoever is fortunate enough to become President of the United States, should have the right to appoint his or her appointees and they should have some ability to influence the culture and practice of that agency. If they don't, they shouldn't be there. They should not be there. Now, so to make a statement that the fact that they are appointees and the fact that they try to manage, that somehow political interference is a pejorative term. They shouldn't be there if they don't try to manage in some way the agencies. Now, on page 3 of your testimony, and you underlined this with a bullet point, you say, "Interference can take many different forms including falsifying data and fabricating results." Can you give any specific examples where a political appointee has flat falsified the data or fabricated results?

Ms. GRIFO. Yes, sir.

Mr. BARTON. Can you give one off the top of your head?

Ms. GRIFO. Off the top of my head, I would say this is an example of both the things that we are talking about. I am thinking of Assistant Deputy Secretary of Interior, Julie McDonald, calling biologists in the field and bullying them into reaching conclusions that——

Mr. BARTON. Wait a minute. Wait a minute. Making a phone call is not——

Ms. GRIFO. Well, let me finish.

Mr. BARTON. Falsifying data is——

Ms. GRIFO. We have her changes, track changes——

Mr. BARTON. You tell me the data point is 10 parts per million and I say no, no, it is not, we are going to put that it is 5 parts per million or we are going to put it as 100. That is falsifying data. Having a difference of opinion or challenging an assumption or a conclusion is one thing, and that may be wrong past a certain point in time, but that is not what you say. You said they falsify data and they fabricate results. Now, if you all can prove that, Mr. Stupak and Mr. Shimkus and myself and Mr. Dingell, we want to know it. I mean, that is fraud.

Ms. GRIFO. Yes, sir. Can I direct you to our A–Z guide to political interference in science? We have nearly 90 examples there of exactly what we mean by political interference. Every single one of them is——

Mr. BARTON. Well, wait a minute. You are changing the terminology. We are not talking about political interference, we are talking about falsifying data.

Ms. GRIFO. Well, that is one of those kinds of——

Mr. BARTON. Fabricating a result, now, that is different. Now, my time is just about up, so I want to put something in the record, Mr. Chairman, and we will give it to the Majority staff before you agree to put it in but I am going to read from it because later on in her testimony the doctor talks about climate change and greenhouse gases and how that has been impacted. I haven't verified this but I want to get your take on it. This is a gentleman named David Evans. He is an Australian scientist, and he participated in the Kyoto Protocol and I am just taking his word so I can't verify under oath this is true. I am going to quote, "I have been following the global warming debate closely for years. When I started the job in 1999, the evidence that carbon emissions caused global warming seemed pretty good. CO_2 is a greenhouse gas. The evidence wasn't conclusive but why wait until we were certain when it appeared we needed to act quickly. Soon the government and the scientific community were working together and lots of science research jobs were created. But since 1999, the new evidence has seriously weakened the case that carbon emissions are the main cause of global warming, and by 2007, the evidence was pretty conclusive that carbon played only a minor role and was not the main cause of the recent global warming. As Lord Kean famously said, when the facts change, I change my mind. What do you do, sir. There hasn't been any public debate about the causes of global warming and most of the public and our decision makers are not aware of the most basic facts. Number one, the greenhouse gas signature is missing. We have been looking and measuring it for years and cannot find it. Each possible cause of global warming has a different pattern everywhere in the planet the warming occurs. The signature of an increased greenhouse effect is a hot spot about 10 kilometers up in the atmosphere over the tropics. We have been measuring the atmosphere for decades using radiosons, which are weather balloons with thermometers that radio back the temperature as the balloon ascends through the atmosphere. They show no hot spot whatsoever. If there is not a hot spot, then an increased greenhouse effect is not the cause of global warming. So we know for sure that carbon emissions are not a significant cause of global warming. If we had found the greenhouse signature, then I would be an alarmist again. When the signature was found to be missing in 2007, after the latest IPCC report, the alarmists objected that maybe the readings of the radioson thermometers might not be accurate. Maybe the hot spot was there but had gone undetected. Yet hundreds of radiosons have given the same answer so statistically it is not possible that they have missed the hot spot. Recently the alarmists have suggested we ignore the radioson thermometers but instead take on radioson wind measurements, apply a theory about wind shear and run the results through the computers to estimate the temperature. Then they say that the results will show that we cannot rule out the presence of a hot spot. If you believe that, you will believe anything." Do you think that the Bush Administration has prevented this information from being public?

Ms. GRIFO. Is that to me?

Mr. BARTON. Yes, ma'am.

Ms. GRIFO. No idea.

Mr. BARTON. Well, do you have an opinion?

Ms. GRIFO. No, not my issue. Climate change is a complicated debate.

Mr. BARTON. Not your issue?

Ms. GRIFO. No, I think——

Mr. BARTON. You talk about patterns of abuse.

Ms. GRIFO. Could I finish?

Mr. BARTON. Scientists studying what may very well be the most profound global change of the century, global warming, are effectively barred from communicating their findings to the news media and the public.

Ms. GRIFO. Well, that I am happy to discuss. I mean, we do have———

Mr. BARTON. That is what I am asking about.

Ms. GRIFO [continuing]. Examples of interference. We do have many examples. I think James Hanson achieved great notoriety.

Mr. BARTON. Do you think that this might be an example of the scientific community not wanting to acknowledge an unpleasant fact, that in fact you can't prove that manmade CO_2 is a cause of global warming and it may be the scientific community whose theory is wrong and so they don't want to publicize this? You know, this isn't OMB preventing this from becoming public or Dr. Johnson at the EPA or some assistant secretary or something.

Ms. GRIFO. The IPCC is a very thorough process, very peer reviewed, very well constructed. It is the gold standard for this information. I am sure that they have considered and deliberated that gentleman's opinion and I am sure——

Mr. BARTON. And I don't know that it is——

Ms. GRIFO. But I don't know that it was suppressed. I have no evidence of that. If you have evidence of that that you would like to——

Mr. BARTON. No, ma'am, I am not the one alleging suppression.

Ms. GRIFO. I am happy to investigate it and add it to our list of examples, if you have that documentation.

Mr. BARTON. Mr. Chairman, I have abused the privileges of the subcommittee in terms of its time commitment.

Mr. STUPAK. I was going to remind you of that.

Mr. BARTON. I will submit this for the record if the Majority and you determine it is worthy of being included, and I do ask our Dr. Grifo to please supply the subcommittee with specific facts and not just opinions and we will investigate those facts and see where they lead.

Thank you, Mr. Chairman.

Mr. STUPAK. Sure, and as to Dr. Grifo and the facts, their report is under tab number 2 and has pretty much very specific examples from former EPA Director Christie Todd Whitman and others, so I think a lot of the stuff you are asking for is probably there. As far as this report on climate change from the Australian newspaper, this really isn't a hearing on climate change but I have no objection if you want to include it in the record.

Mr. BARTON. Well, if there is no objection, I would like it to be in the record, but I cannot verify that what it says is totally true but it is something we need to look into.

Mr. STUPAK. Right. Maybe we ought to have Mr. Evans come here on a climate change hearing.

Mr. BARTON. That might be a good idea.

Mr. STUPAK. Thanks.

Mr. STUPAK. Mr. Inslee for questions, please.

Mr. INSLEE. Yes, that author of that report that Mr. Barton is quoting could arrive on his UFO that he has told us about as well. If the definition of successful political appointees are ones that do in fact affect science, then this Administration has been supremely successful. There is no question about that, because they have suppressed it every chance they can and it is pretty obvious it has gone on. We have seen it on multiple occasions from Julie McDonald on up, and it is perverted science and it has perverted what the taxpayers have paid for and I don't really even think we need a study to know that. If you talk to people at the EPA like I do, you just simply know that. When I get on the ferry boat and talk to my neighbors who work for the EPA, you know that, and you know it from the sort of macro view. You know it because in December of 2007, the EPA scientists essentially recommended allowing States to limit greenhouse gases from cars and trucks and then the political appointees deny that and refuse to allow that to happen. Now, we know that. There is no dispute about this. The scientists made a recommendation. The political appointees denied it. It is out in the open, and that is a fraud and that is a travesty and that is a rejection of science that is right out in the open. We don't even have to have surveys about it. July 11, 2008, the EPA political appointees decided not to take any steps to regulate greenhouse gases despite the fact they have been ordered to do so if it affects human health. They have concluded it does, but right out in the open, this was a bank robbery out in the open, this wasn't at night. I mean, and I really respect the people who work for the EPA who are trying to do their jobs under these very, very difficult situations, and I just want to tip my hat to them. It would be so easy to be totally demoralized to do good science, to give it and then have it squashed by the Bush Administration must be very difficult for them and I want to honor them, and I want to tell you why I am so concerned.

If somebody would put up this picture here, my staff can help me, a little picture of what is at stake here. This is a photograph of the—actually a graphical representation of satellite information of the poles, the Arctic basically showing the summer ice, the September ice in the upper left-hand corner showing September 1979. The sort of light blue is what is called the very new ice, the very, very thin ice, and the white is the permanent ice, the long-term ice. Then you go to down below that to September 1989, you see a very significant reduction in the permanent or essentially long-term ice. You go up in the right-hand corner, you will see September 1999, a continued reduction, and this is what is stunning. September 2007, the bottom right-hand corner, the only new ice are just basically little tiny vestigial remnants of the white down at the bottom. We have had an absolute collapse of the Arctic while we are sitting here debating about whether the Administration has suppressed science in the EPA or not. It is pretty doggone clear that this Administration has suppressed the single-most important scientific inquiry probably in human history in this issue of how rapidly this is happening, and I want to show this because this is grounded in the real world. In the Arctic, if people understand how important this is, this is the heat shield for the planet. John Glenn, if you remember when he came in, he had the heat shield. It shielded him. This is the heat shield for the planet earth because it reflects massive amount of radiation when there is snow there, but when there isn't ice there, the ocean absorbs the energy, and this is a tipping point potentially that the scientists are so concerned about.

So to me, I appreciate our two witnesses today but it is so obvious that the Administration has suppressed and ignored scientists that it is not a survey that is private, it is a public rejection of science that we have witnessed, and it portends potential fairly cataclysmic results, and I am astounded that we are still having these discussions, but we are, and I just look forward to January 20, 2009, when this country can get back to the job of science. If anybody wants to comment on that, go ahead. Anybody want any comment?

Ms. GRIFO. Touche.

Mr. INSLEE. Thank you.

Mr. STUPAK. All right. Mr. Shimkus has a question.

Mr. SHIMKUS. Just one follow-up. Dr. Grifo, you mentioned the names of the peer reviewers who did your report. Were any of those inside of your organization that were not outside?

Ms. GRIFO. Two.

Mr. SHIMKUS. And can you name the two?

Ms. GRIFO. I think it was Kathy Rest and Michael Halpern.

Mr. SHIMKUS. Kurt Gottfried.

Ms. GRIFO. Kurt is not inside. He is on our board but he is a physicist——

Mr. SHIMKUS. He is not just on the board, he is the chairman.

Ms. GRIFO. He is, but he is also a physicist at Cornell University.

Mr. SHIMKUS. So there are three?

Ms. GRIFO. Yes. Well, about your definition of inside, but I will grant you that——

Mr. SHIMKUS. That is our problem. Yes, is that typical for peer-reviewed scientific reports to be peer reviewed by people within the organization?

Ms. GRIFO. It is very typical for people within an organization to comment on a report. They are included in the list——

Mr. SHIMKUS. But to use that as the official peer review?

Ms. GRIFO. There are other names on that list that are not within the organization that are part of the official peer review. I was talking about the review of the documents in general since——

Mr. SHIMKUS. As you know, we have problems with your presentation today.

I yield back. Thank you, Mr. Chairman.

Mr. STUPAK. Let me ask this question, and I will ask either Mr. Stephenson or Dr. Grifo. Peer review, explain it, what does it do, peer review?

Mr. STEPHENSON. She is the scientist.

Mr. STUPAK. OK. It is my understanding you gather information. You are asked to look at it. You gather information and then you do your individual assessment. In this case, it would go, let us say, to the EPA and the EPA would draw conclusions based upon the peer review. It is not unusual for a peer review panel to have someone who may be in the industry, outside the industry, academia. Is that basically a peer review? You get people from all over, some whom might come with some preconceived bias on this chemical and some who would be just the opposite and academia and they look at the unisphere or the universe of information and then they make an assessment and they submit it to the Agency. It is the Agency that makes the final decision, correct?

Ms. GRIFO. Yes. I think what is important is to distinguish between scientific advisory committees and scientific review versus a stakeholder committee, and I think we have both kinds of committees that are out there considering information and advising agencies. I think on a stakeholder committee, you do in fact have multiple points of view, you know, you do have conflicts of interest. People are representing industry, representing different aspects of society, but the key is that a stakeholder panel should not make scientific judgments. I think the topic that we have been dancing around here is that there is a difference between scientific conclusions and a political decision, a policy decision. "Political" may be too loaded a word, a policy decision, and I think the root of the problem that we have seen at EPA and multiple other agencies is the firewall that should be between those decisions has come down. You don't interfere with the science. You take the scientific conclusions, as a policymaker you can ignore them if the statutes will allow you.

Mr. STUPAK. So the peer review would look at the information, give it to the policy side and policy decision makers make the decision?

Ms. GRIFO. Depending on the statute that is governing. But I think the other thing is, on a strictly scientific review panel, you do want to look at conflict of interest, you want to look at financial connections. It is a very different kind of a group of people that is convened for a different purpose.

Mr. STEPHENSON. Could I add, from a layman's point of view, the peer reviewer is there to assert to the reasonableness of the scientific approach. There are very specific rules governing the makeup of peer review panels that they must be balanced, so you don't have to be a scientist to understand the rules of peer review. You can argue with whom is on the peer review but all agencies and all scientific organizations that use peer reviewers are very careful about making sure there is a balanced makeup across that, and EPA is as well.

Mr. STUPAK. So a peer review panel would look at this document that Mr. Barton put in the record, the Australian, and Mr. David Evans, who disagreed with global climate change, if they were looking at climate change, they might include that one or they might——

Mr. STEPHENSON. Well, the IPCC would look into the basis for that conclusion, the evidence that he used to draw that conclusion and talk about the reasonableness of that.

Mr. STUPAK. And one person may submit it in their assessment where another peer review person may not?

Mr. STEPHENSON. The peer reviews try to come to consensus. They are expected to have divergent views. But in the end, there are safeguards that the approach used for the science is in fact reasonable.

Mr. STUPAK. Mr. Shimkus?

Mr. SHIMKUS. Mr. Chairman, I would just say that, and some of the testimony talked about it, it being public and external, at least for the EPA. I would think it would be more accurate to identify those peer review people who are internal to the organization versus those who are external to the organization, and again, my problem with this whole debate is that the accusations that are lobbed at the EPA, I would submit are the same accusations that can be lobbed at this report that you presented and it is very hard for—you just can't have it both ways.

Ms. GRIFO. Could I respond?

Mr. STUPAK. Quickly.

Ms. GRIFO. One sentence. In the paragraph in the acknowledgements, it talks about how those people provided comment. We do not use the words "peer review" in referring to them. That was my answer to your question.

Mr. SHIMKUS. Not being specific. I mean, that is the whole point of this whole frustration. You called them peer review. You named them out and they are part of your organization.

Ms. GRIFO. You asked me.

Mr. STUPAK. All right. We have two frustrated people now in the room and that is it, it is not getting any bigger, so why don't we do this? Let us dismiss this panel. We have two votes on the floor. We will take a break here. Let us go vote and we will come right back, or do you want to do the testimony of the next panel? We have four people on there. We would never get in.

All right. Let us adjourn for recess for two votes. Hopefully we are back here by 20 after, OK, so 12:20. We stand in recess.

[Recess.]

Mr. STUPAK. We will reconvene this hearing. I thank everyone for your patience while we had a few votes on the floor there. The second panel of witnesses that we have now is Dr. Deborah Rice, who is the Epidemiologist at the State of Maine's Department of Environmental Protection; Dr. Jennifer Sass, who is Senior Scientist at the Natural Resources Defense Council; Mr. Daniel Parshley, who is Project Manager at the Glynn Environmental Coalition in Brunswick, Georgia, and Ms. Sharon H. Kneiss, who is Vice President of Products Division at the American Chemistry Council.

It is the policy of this subcommittee to take all testimony under oath. Please be advised that you have the right to counsel during your testimony. Do any of you wish to be represented by counsel? Everyone is shaking their head no. Ms. Kneiss?

Ms. KNEISS. Chairman, I do have counsel with me.

Mr. STUPAK. They can advise you but not testify, OK? And if you do consult him, we may ask who the name is at that time. All right. I am going to ask you to take the oath, so if you able to, raise your right hand.

[Witnesses sworn.]

Mr. STUPAK. Let the record reflect that the witnesses have taken the oath. They are now under oath. We will hear an opening statement for 5 minutes, please. If you have a longer statement, just submit it for the record. It will be made part of the official record. Dr. Rice we will start with you, please.

STATEMENT OF DEBORAH RICE, PH.D., STATE OF MAINE, DEPARTMENT OF ENVIRONMENTAL PROTECTION

Ms. RICE. Mr. Chairman, members of the committee, my name is Dr. Deborah Rice. I am a toxicologist with over 30 years of experience in basic research and risk assessment. I am currently employed by the Maine Center for Disease Control and Prevention. I previously served as a senior risk assessor in the National Center for Environmental Assessment at the U.S. Environment Protection Agency, which by the way is the home of the IRIS program.

I am here today to outline the events related to my removal from an expert panel reviewing an EPA assessment for four polybrominated diphenyl ether flame retardants, so-called PBDEs, and to offer my perspective on the events. To do that, I need to describe my activities as part of my professional duties for the State of Maine. In 2004, the Maine Legislature approved a presumptive ban on one flame retardant, deca BDE, pending a series of annual reports by State professional staff on the health and environmental hazards of deca BDE and potential available alternatives. I contributed to three reports in 2005 to 2007 and spoke before the relevant legislative committee regarding the Maine bill. In that capacity, I conveyed my scientific opinion on the hazards of deca BDE compared to possible alternatives.

In December 2006, EPA published a draft document for four individual forms of PBDEs, including deca BDE. This document consisted of a scientific review of the health effects and derivation of a safe intake level, the so-called reference dose, for each of these individual PBDEs. There is no consideration in this type of document of banning a chemical or of its use in specific products. I was invited to chair the external panel convened to review this document by the independent contractor responsible for organizing the peer review. The panel met in February 2007. My function as chair was to ensure that all scientific issues were discussed and all reviewers had an opportunity to express their views. There is no requirement for reviewers to reach consensus. The final comments of each peer reviewer were posted on the EPA Web site in March 2007.

In May 2007, I received a telephone call from Dr. George Gray informing me that EPA had received a letter from the American Chemistry Council requesting that I be removed from the panel on the grounds that my comments in Maine concerning deca BDE reflected bias. The ACC further argued that they disagreed with the results in a scientific research paper that I coauthored published subsequent to the EPA review. Dr. Gray questioned me concerning my activities in Maine and indicated that he was considering acquiescing to industry's request. A later phone call informed me of that decision. I did not receive any written notification that I was being removed from the panel. I was told that only my comments on deca BDE would be removed. In fact, my comments for all four chemicals were removed from a revised peer review report published in August and my name erased from the document. In September, EPA published a third version of the document which added a statement requested by the American Chemistry Council that "one reviewer's comments were excluded from the report due to the perception of a potential conflict of interest," a statement also currently on the EPA IRIS Web site. The final version of the EPA toxicological review included my name as a peer reviewer but does not include response to my comments.

There are several points that I think are relevant to interpreting the validity of my removal from the peer review panel by EPA.

First, my professional activities for the State of Maine were required as part of my duties as the toxicologist charged with providing expert scientific opinion to State legislators. I had no opinion on the hazards posed by deca BDE before I started my review. I believe that having an informed scientific opinion constitutes neither bias nor conflict of interest. Indeed, if this is the definition of bias, then only individuals who are uninformed on a particular chemical would be considered suitable to serve as peer reviewers.

Second, the bill before the Maine Legislature and the EPA document on the derivation of reference doses address different issues. The Maine bill dealt with whether safer chemicals were available as substitutes for one specific flame-retardant chemical. The EPA document addressed derivation of a safe level of ingestion over a life span for four of these chemicals. My view that safer chemicals were available did not reflect on my ability to follow the EPA protocol for derivation of a reference dose. I am very familiar with the process, having worked as a senior risk assessor for EPA. In addition, EPA regards these chemicals as hazardous or it would not have derived reference doses for them.

Third, I believe my comments and recommendations were objective and based on my 30 years of expertise as a toxicologist. To give an example, in initial comments I was the only reviewer to be critical of a specific feature of the experimental design of the studies upon which the EPA derivations were based. The identical argument was made by the ACC in their comments to EPA. The only evidence provided by the ACC that I performed in a biased manner with regard to the peer review was that they disagreed that deca BDE produces a specific health effect.

I thank the Committee for the opportunity to discuss this issue.

[The prepared statement of Ms. Rice follows:]

STATEMENT OF DEBORAH RICE

My name is Dr. Deborah Rice. I am a toxicologist with over 30 years of experience in basic research and risk assessment. I am currently employed by the Maine Center for Disease Control and Prevention. I previously served as a senior risk assessor in the National Center for Environmental Assessment at the U.S. Environmental Protection Agency.

I am here today to outline the events related to my removal from an expert panel reviewing an EPA assessment of four polybrominated diphenyl ether flame retardants (PBDEs), and to offer my perspective on the events. To do that, I need to describe my activities as part of my professional duties for the State of Maine. In 2004, the Maine legislature approved a presumptive ban on one flame retardant, deca BDE, pending a series of annual reports by state professional staff on the health and environmental hazards of deca BDE and potential available alternatives. I contributed to three reports in 2005 092007, and spoke before the relevant legislative committee regarding the Maine bill. In that capacity I conveyed my scientific opinion on the hazards of deca BDE compared to possible alternatives.

In December, 2006, EPA published a draft document for four individual forms of PBDEs, including deca BDE. This document consisted of a scientific review of the health effects and derivation of a safe intake level (reference dose) for each of these individual PBDEs. There is no consideration in this type of document of banning a chemical or its use in specific products. I was invited to chair the external panel convened to review this document by the independent contractor responsible for organizing the peer review. The panel met in February 2007. My function as chair was to ensure that all scientific issues were discussed, and all reviewers had an opportunity to express their views. There was no requirement for reviewers to reach consensus. The final comments of each reviewer were posted on the EPA Web site in March 2007.

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Third, I believe my comments and recommendations were objective and based on my 30 years of expertise as a toxicologist. To give an example, in initial comments I was the only reviewer to be critical of a specific feature of the experimental design of the studies upon which the EPA derivations were based. The identical argument was made by the ACC in their comments to EPA. The only evidence provided by the ACC that I performed in a biased manner with regard to the peer review was that they disagreed that deca BDE produces a specific health effect.

I thank the Committee for the opportunity to discuss this issue.

Mr. STUPAK. Thank you, Doctor.

Dr. Sass, your opening statement, please.

STATEMENT OF JENNIFER SASS, PH.D., SENIOR SCIENTIST, NATURAL RESOURCES DEFENSE COUNCIL

Ms. SASS. Good afternoon, and thank you for the opportunity to testify on the failure of the EPA IRIS program to serve the needs of the public. My name is Jennifer Sass and I am a Senior Scientist in the health program at the Natural Resources Defense Council. I worked there for 8 years. I have a scientific background in toxicology, developmental biology, and neurotoxicology, and my task with NRDC is primarily to review and assess the science that underlies the regulation of hazardous chemicals.

We commend the subcommittee for its interest in the EPA IRIS review process and its oversight of recent changes made to the program. IRIS is a cornerstone program at EPA which provides the scientific information necessary to develop our Nation's air and drinking water standards as well as hazardous cleanup levels. It is the program that evaluates the scientific evidence available on the potential for chemicals to cause harm to human health.

The Administration's record of political interference with the work of government scientists across a range of environmental issues including global warming and endangered species has been well documented. Things are no better in the case of analyzing and regulating toxic chemicals that pose a risk to human health. In this area, the Administration has attempted and in some instances succeeded to block, weaken, or delay health standards for a long list of dangerous pollutants including the pesticides atrazine and carbofurin, the rocket fuel additive perchlorate, and formaldehyde. Not content to simply undermine health hazards for a host of toxic chemicals one by one, the Administration officials have now set their sights on the foundational process for assessing the risks of toxic chemicals, the EPA Integrated Risk Information System, or IRIS, that assesses hazardous substances. The new 2008 IRIS process introduces three new opportunities for the White House Office of Management and Budget and other non-health agencies such as the Department of Defense and the Department of Energy to comment on EPA's health assessments where previously there has been only one opportunity. Thus, where the pre-2004 IRIS process provided the agencies and OMB with the draft assessment at the same time as it was provided to the public, the new process invites the other agencies into the assessment process at an earlier stage and obligates the IRIS staff to address the queries of the agencies and OMB whether or not they are consistent with health-protective policies. Following this negotiation, the draft review is then publicly noticed, but then there is a final intervention point provided to OMB and the other agencies that requires IRIS staff to resolve any outstanding concerns by OMB and the other agencies including polluting agencies before the assessment can be finalized.

While the 2008 process boils down to death by a thousand cuts, this ability to have the last word and to potentially axe an assessment at the bitter end may be the deepest cut of all. Although current EPA management argues that the new process was developed to provide greater transparency, objectivity, balance, rigor, and predictability to the IRIS assessments, this new process gives the polluting agencies more access and more influence to what has historically been a reasonably objective scientific evaluation process. The new process established by the White House invites interference by OMB and other agencies at the outset of the process, in the middle, and at the end. Importantly, the Administration has sought to classify these newly introduced intervention points as deliberative and hence shield them from public view, and alarmingly, the new opportunities are not limited to data critiques. One particularly misguided new feature offers agencies outside of EPA up to 2 years to undertake their own studies of mission-critical chemicals, potentially suspending EPA's evaluation of these contaminants for a very substantial period of time.

The IRIS program has always struggled to keep pace with EPA's regulatory needs and many environmental contaminants lacking IRIS assessments are quite important to public health. For instance, there is no IRIS assessment for nearly one-third of the 189 pollutants listed as hazardous under the Clean Air Act. Furthermore, even when important chemicals are in the IRIS database, the risk assessments for many of these are outdated. The average IRIS assessment is over 13 years old. The oldest one has not been significantly revised since the mid-1980s. These problems greatly exacerbate the already long period of time required for EPA standard-setting procedures, up to a decade in some cases, and have been the focus of criticism for some time. Clearly, constructive reform of the IRIS program would focus on increasing resources available to undertake IRIS reviews as well as policy changes that would streamline the difficult decisionmaking inherent in the process. Properly managed, the EPA IRIS program provides a critical scientific service to the public. Speed is important but scientific quality and integrity is paramount.

Another example of politics trumping science is the recent dismissal by EPA of one of their most respected and credible scientific reviewers, Dr. Rice, in response to a written request from the Brominated Flame Retardant Industry Panel of the American Chemistry Council. A notice posted on EPA's Web site states that the exclusion is because due to the perception of a potential conflict of interest. The way EPA management has applied the peer review guidelines and expert scientists like Dr. Rice could be disqualified by taking a public position supporting the phase-out of chemicals where scientific evidence is mounting that they are persistent, biocumulative, and toxic and in cases where safer alternatives are available. This position is not in conflict with the scientific consensus among public health experts and it is not in conflict with many State public health agencies where some PBDEs have been banned or restricted. The only potential conflict that Dr. Rice seems to have is with the American Chemistry Council and their member companies that manufacture PBDEs. These groups continue to defend the chemicals and testify against State bans.

In a book recently issued by David Michaels, former Assistant Secretary of Energy, titled "Doubt Is Their Product: How Industry's Assault on Science Threatens Your Health," the author emphasizes that the failures of EPA to regulate hazardous materials are not the fault of most agency scientists or career employees, many of whom are heartsick that their work has been so undermined.

We requested this subcommittee and full committee work with colleagues to defend our public servant scientists as the Nation's brain trust. Thank you.

[The prepared statement of Ms. Sass follows:]

TESTIMONY OF
JENNIFER SASS, Ph. D
SENIOR SCIENTIST
NATURAL RESOURCES DEFENSE COUNCIL

ON BEHALF OF:
NATURAL RESOURCES DEFENSE COUNCIL

BEFORE THE U.S. HOUSE
COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS[1]

AT HEARING ENTITLED:
SCIENCE UNDER SIEGE: SCIENTIFIC INTEGRITY AT THE ENVIRONMENTAL PROTECTION AGENCY

September 18, 2008

One-Page Summary

September 18, 2008

Testimony of Jennifer Sass, Natural Resources Defense Council, before the US House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, at hearings entitled: *Science under Siege: Scientific Integrity at the U.S. EPA*

Throughout the eight years of the Bush Administration, NRDC has documented the science under siege at the EPA, to expose the chemical industry's campaign to destroy EPA's technical infrastructure and policy framework.

Not content to simply undermine health standards for a host of toxic chemicals one-by-one, Administration officials have also attacked the foundational process for assessing the risks of toxic chemicals, the EPA Integrated Risk Information System (IRIS) program that assesses hazardous substances. The new 2008 IRIS process introduces three new opportunities for the White House Office of Management and Budget (OMB) and other non-health agencies to weigh in on EPA's health assessments, where previously there was only one. Importantly, interagency comments and OMB comments for all three of the new intervention points are shielded from public view. Thus, whereas the pre-2004 IRIS process provided the agencies and OMB with the draft assessment at the same time as it was provided to the public, the new process invites polluting agencies such as the Department of Defense (DOD) and the Department of Energy (DOE) into the assessment process at an earlier stage, and forces the IRIS staff to address the queries of the agencies and OMB, whether or not they are consistent with health-protective policies; these exchanges are not publicly accessible. Following this negotiation, the draft review is publicly noticed. But then there is a final intervention point provided to OMB and the other agencies that require that the IRIS staff to resolve any outstanding concerns by OMB and the other agencies, including polluting agencies, before the assessment can be finalized. While the 2008 process boils down to 'death by a thousand cuts,' this ability to have the last word – and to potentially to axe an assessment at the bitter end -- may be the deepest cut of all. Although current EPA management argues that the new process was developed in order to provide 'greater transparency, objectivity, balance, rigor and predictability' to the IRIS assessments, this new process gives the polluting agencies more access and more influence to what has historically been a reasonably objective scientific evaluation process.

Another example of politics trumping science is the recent dismissal by EPA of one of their most respected and credible scientific reviewers, Dr. Rice, in direct response to a written request from the Brominated Flame Retardant Industry Panel (BFRIP) of the American Chemistry Council.

Good morning and thank you for this opportunity to testify on science under siege at the Environmental Protection Agency. I am Jennifer Sass, PhD., a Senior Scientist at the Natural Resources Defense Council (NRDC). I work in the Health and Environment Program, which reviews the federal regulation of industrial chemicals and pesticides. Over my eight years with NRDC, I have published over two dozen articles in scientific journals, provided written and oral testimony to Congress, to the Environmental Protection Agency and to the National Academies, as well as served on Federal scientific and stakeholder committees. I completed post-doctoral studies in toxicology at the University of Maryland, doctoral studies in developmental biology, and a master's thesis in neurobiology at the University of Saskatchewan.

The Natural Resources Defense Council (NRDC) is a national, nonprofit organization of scientists, lawyers and environmental specialists dedicated to protecting public health and the environment. Founded in 1970, NRDC has 1.2 million members and online activists, served from offices in New York, Washington, Chicago, Los Angeles, San Francisco and Beijing.

NRDC's Health program focuses on toxic chemical pollutants in air, water, food, and shelter. Over the years, we have focused our particular attention on the "biggest pollutants" in these media, the ones disproportionately responsible for the biggest threats to human health. This has led to successful efforts to substantially reduce diesel air emissions from trucks and buses, for example, and to take a number of dangerous and outdated pesticides off the market. There are more than 70,000 chemicals in commerce, but some are much more toxic than others, and we can make great progress in environmental health protection if we focus on the chemicals pollutants that pose the greatest threat to human and ecological health.

Throughout the eight years of the Bush Administration, NRDC has documented the science under siege at the EPA, to expose the chemical industry's campaign to destroy EPA's technical infrastructure and policy framework.[2] Evidence of industry's efforts include attempts to weaken EPA assessments of vinyl chloride carcinogenicity,[3] the effects of low levels of the rocket fuel perchlorate,[4] [5] and environmental impacts of the pesticide atrazine[6], as well as actions taken by the Office of Management Budget (OMB) on formaldehyde, which ultimately led to an EPA assessment that was several thousand times weaker than EPA staff recommended.[7]

We are very pleased to testify today on scientific integrity issues at the Environmental Protection Agency (EPA), particularly as these issues relate to the scientific assessment of health risks posed by exposure to hazardous chemicals. Efforts of the chemical manufacturing industry to bias the scientific reporting on the hazards of their products have long been documented. [8] [9] [10] Over the past eight years, the industry has broadened its attack on EPA science with the assistance of EPA's political appointees:

- blocking, delaying or weakening individual health standards,

- undermining the fundamental program that establishes the level of risk posed by toxic chemicals, and
- attacking the objectivity and credibility of independent and government scientists, while shamelessly promoting the supposed objectivity of industry scientists and consultants, many with direct financial conflicts in the matters they are reviewing.

These efforts to interfere with good science at EPA are the focus of our testimony to the Committee today.

OMB-IMPOSED ALTERATIONS TO IRIS PROCESS OF HAZARDOUS CHEMICAL EVALUATIONS UNDERMINE A PROGRAM CRITICAL FOR PROTECTING PUBLIC HEALTH

Not content to simply undermine health standards for a host of toxic chemicals one-by-one, Administration officials have also attacked the foundational process for assessing the risks of toxic chemicals, the IRIS program. The recent changes to the IRIS process that are the subject of today's hearing should properly be viewed as one part of a much broader agenda to sacrifice public health protections and limit public understanding of the risk of toxic chemicals, in a manner that benefits a host of polluting industries and federal agencies. Indeed, by attempting to weaken the IRIS process, the Administration has zeroed in on one of the earliest and most fundamental steps in the process of protecting public health, that in which EPA's scientists identify the health risks posed by exposure to certain chemicals. The committee's hearings should preface Congressional action to reverse the recent changes to the IRIS process and ensure the integrity and effectiveness of the program is restored.

The importance of the IRIS database

The IRIS database is a publicly available database which contains EPA's evaluation of potential human health effects from exposure to more than 540 chemicals, including highly hazardous chemicals such as PBDE's (polybrominated diphenyl ethers, a class of flame retardants), vinyl chloride, butadiene, benzene, lead, mercury, and asbestos.[11] While these evaluations are not regulations *per se*, they are used by both state and federal regulators and by the international community for a range of environmental health regulation and management purposes. For example, the information can be used in combination with exposure data to set cleanup levels at hazardous waste sites, or to set exposure standards for air, water, soil, and food. Thus, the accuracy, credibility, and timeliness of IRIS assessments have real world consequences for human health.

The global importance of this database cannot be overstated. For example, last month (August, 2008), the IRIS website received over 27,000 visits (an average of over 885 per day), from over 3,000 distinct computer sources over 60 countries around the world.[12]

IRIS conducts scientific assessments, not policy documents

Risk assessments involve the integration of hazard identification, dose-response assessment, and exposure assessment to estimate the probability (likelihood) of harm.

Rather than conducting entire risk assessments, the IRIS program is limited to conducting hazard identification and assessing dose-response relationships for environmental chemicals; EPA factors in exposure scenarios and risks under its regulatory programs.

Hazard identification, the first step in a risk analysis, determines whether or not the substance of concern is likely to have adverse health effects. This step requires a thorough review of relevant toxicologic data and may include human epidemiology, whole animal studies, non-animal data, and field data. The result is a scientific determination of whether or not a substance causes adverse health outcomes such as cancer, neurological disease, birth defects, or death. Since reliable human data is often not available, hazard evaluations generally rely heavily on identifying whether the substance is toxic in animals or other test systems.

The dose-response assessment follows hazard identification and is designed to identify safe levels of exposure for chemicals that pose harm. This assessment consists of scientifically characterizing the relationship between the amount of exposure (dose) and the incidence of an adverse health endpoint. Methodologies for dose-response assessment often differ between cancer and non-cancer effects and between acute and chronic exposure scenarios. They are often scientifically controversial, because they must extrapolate from high experimental doses to more typical ambient exposure levels.

Ideally, epidemiological data would be available that clearly illuminate the hazards and the dose-response relationships for chemicals of concern in human populations. Unfortunately, this is nearly never the case. Most chemicals lack key studies of effects in humans as well as studies of effects in animals at ambient levels. As a result, IRIS assessors are called upon to make informed judgments regarding the relevance of the animal data to humans, and to select the most appropriate extrapolation method. Further, the IRIS assessments require independent expert judgment to decide whether various safety factors should be applied to assessment data to ensure public health protection. For example, EPA often decides to include margins of safety to protect vulnerable populations, relevant genetic variations, vulnerable life stages, disease states, concomitant exposure to complex mixtures, and other relevant factors that may influence the probability of an effect caused by exposure to the substance of concern.

Importantly, decisions made in the IRIS program are informed by various EPA guidance documents that are publicly-available and publicly-documented, and have been publicly-vetted. Reliance on these important guidance documents is crucial to ensure that evaluations are consistent across substances and as objective as possible.

The new process established by the White House turns this process on its head: it invites the injection of non-scientific considerations into the IRIS assessments, and further, it shields from public scrutiny the input from other parts of the government with a potential financial or political interest in the outcome of a particular assessment. When political appointees, perhaps acting on behalf of regulated industries, and polluting agencies are able to interfere in a non-transparent and inappropriate manner, the whole process is severely compromised.

Summary of the new process

The new 2008 IRIS process introduces three new opportunities for OMB and other non-health agencies to weigh in on EPA's health assessments, where previously there was only one. Importantly, interagency comments and OMB comments for all three of the new intervention points are shielded from public view: the first two bites at the apple, and the last one. Thus, whereas the pre-2004 IRIS process provided the agencies and OMB with the draft assessment at the same time as it was provided to the public, the new process injects polluting agencies such as DOD and DOE into the assessment process at an earlier stage, and forces the IRIS staff to address the interests of the agencies and OMB, whether they are consistent with health-protective policies or not. These exchanges take place out of the public eye. Following this negotiation, the draft review is publicly noticed. But then there is a final intervention point provided to OMB and the other agencies that require that the IRIS staff to resolve any outstanding concerns by OMB and the other agencies, including polluting agencies, before the assessment can be finalized. While the 2008 process boils down to 'death by a thousand cuts,' this ability to have the last word – and to axe an assessment at the bitter end -- may be the deepest cut of all.

The U.S. Government Accountability Office (GAO) recently released its review of the new process, in a report entitled: *Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information*

System.[13] This report provided a detailed and highly critical assessment of the failures of the IRIS program to meet its deadlines and requirements, blaming in large part the interference by polluting agencies and political appointees. The GAO report predicts that the new process will produce IRIS assessments that lack credibility, and will worsen what is already a critical backlog of new and updated assessments. NRDC agrees with the GAO evaluation, whose many findings validate our years of work to right this cornerstone program for public health protection.

For many years, IRIS assessments were developed by EPA scientists. Drafts were released simultaneously for public comment and external (independent expert) peer review. OMB and government agencies such as DOD or DOE, who sometimes had a stake in the outcome of the evaluation because of their obligations to address contamination at federal facilities, had an opportunity to review and comment on the draft when it was released for public review and comment.

Table 1: A comparison of the new and previous (pre-2004) process to conduct and review chemical assessments for the IRIS program

NEW PROCESS	COMPARISON WITH PREVIOUS PROCESS
Scientific literature review (60-90 days)	No significant change
Data call-in (45-60 days)	New
IRIS staff develops a Draft Qualitative Assessment (without any quantitation)	New. In the past, qualitative and quantitative assessments had been presented together; the new process adds an extra assessment to the review cycle
Draft Qualitative Assessment must pass ORD clearance	New

Draft Qualitative Assessment must undergo Inter-Agency review and comments. Comments are deliberative.	New. Note that neither the draft nor the agency comments are publicly accessible and that Inter-Agency review is not restricted to health agencies.
Public release of Draft Qualitative Assessment for public and interagency review and comment (45-60 days)	New
Federal Agencies identify mission critical chemicals	New
Interagency evaluation to close data gaps for mission critical chemical: Agencies can submit a research plan for 'closing data gaps' for mission critical chemicals (90 days)	New
Proposed research and peer review conducted for mission critical chemical; development of new studies (up to 540 days)	New
IRIS staff completes Draft IRIS Toxicological Review (both qualitative and quantitative chapters), addressing public and interagency comments (120-270 days)	No significant change
Interagency review (45-105 days) For mission critical chemicals, EPA cooperates with other agencies to determine peer review process (eg, NAS, SAB); OMB/Interagency review of peer review charge	New
External (independent expert) peer review and public comment (120-280 days)	No significant change
IRIS staff address peer review and public comments, revises IRIS Tox Review and develops IRIS Summary (120-150 days)	No significant change
IRIS staff initiates final OMB/ interagency review and approval of IRIS Tox Review and IRIS Summary (30-45 days)	New to include OMB and interagency approval at this point.
IRIS staff addresses and resolves OMB/interagency remaining issues in consultation with OMB and other agencies. EPA makes final decision.	New to include OMB consultation and approval at this point. Used to be Agency review and clearance only.
EPA completes IRIS Tox Review and IRIS Summary (60 days)	No significant change

The new IRIS process introduces significant new steps that are both time-consuming and undermine the objectivity and transparency necessary for credible and valid assessments (see Table 1). Significant aspects of the new process are as follows:

1. In the 2008 process, IRIS staff is now required to develop a qualitative draft assessment, prior to the quantitative assessment, which must undergo both public and interagency review. This qualitative draft serves as a summary of the scientific literature that the staff intends to rely on to supports its assessment. Although this procedure sounds benign, it seriously compromises the timeliness and transparency of the IRIS program. First, it allows other government agencies to delay an assessment for nearly two years to do additional research on any chemicals that an agency deems to be "mission critical," thereby significantly stalling the start of the formal IRIS evaluation. Even more alarming, the comments and submissions of the other agencies to the qualitative draft are considered 'deliberative' which, if unchallenged or upheld by the courts, would shield the comments from public scrutiny.

2. In the new 2008 process, agencies outside of EPA are invited to designate chemicals as 'mission critical' and to intervene in the IRIS assessment of these chemicals. Mission critical chemicals are defined as those that are, "an integral component to the successful and safe conduct of an Agency's mission in any or all phases of its operations. Impacts on use of mission critical chemicals include cessation or degradation of the conduct of the mission and/or unacceptable resource constraints." [emphasis added] In other words, "mission critical" chemicals includes not only those that are vital and have no viable substitute, but also those where the potential cost to an agency of cleaning up a pollution mess it (or its contractors) have created is "unacceptable" or where potential future

limitations on use (such as stricter exposure standards) are deemed too expensive by the agency. These are exactly the kinds of policy considerations that should *not* be allowed to intrude on the IRIS assessment process.

3. Following the quantitative draft, the IRIS staff develops the draft quantitative assessment (the Toxicological Review). This is subjected to public and interagency review, followed by external (independent expert) peer review. The important difference is that prior to 2004, this represented the first and simultaneous opportunity for both the public and the other agencies to comment, with all comments publicly accessible. By contrast, with the 2008 process this is now the second public comment opportunity, and the third OMB/interagency intervention point, but the first where the OMB/interagency comments would be publicly accessible.

4. Finally, before the IRIS assessment can be finalized and publicly released, the 2008 process requires OMB and interagency approval. The pre-2004 process had only required internal agency review. This 2008 process invites the fourth and final opportunity for OMB/interagency interference with the evaluation. Although the new process says that EPA has the power to make the final decision, it is clear that the other agencies and OMB will have significant access and influence over the final editing choices.

Although current EPA leadership argues that the new process was developed in order to provide "greater transparency, objectivity, balance, rigor and predictability'[14] to the IRIS assessments, we strongly disagree. In fact, the administration's claims are Orwellian. This new process is designed precisely to give the polluting agencies more access and more influence to what has historically been an objective scientific evaluation process -- and to add at least two or more years to the review of mission critical chemicals.

To put it plainly, in this new proposal the Administration is attempting to provide those agencies with the most at stake in the degree of protection established for a particular chemical multiple opportunities to weigh-in and influence the outcome of EPA's decisions, while hiding the exercise of that influence from the public. The Administration's claim that, for example, providing the Department of Defense multiple opportunities to weaken or delay setting a health standard for trichloroethylene (TCE) -- a chemical for which DOD is responsible of widespread contamination of drinking water -- completely outside of public view, will result in a more balanced and objective result, doesn't pass the laugh test.

The EPA leadership further claims that the outcome of the new process is expected to 'streamline' the IRIS process and make it more 'transparent'. Again, we strongly disagree. The new process allows public review at only one stage, which is review of the qualitative draft. All other evaluation steps occur behind closed doors, shielded from accountability to the public or other more objective, outside scientific experts.

It is indicative of the Administration's disregard for public input on its changes to the IRIS process, and its eagerness to put them in place, that OMB admonished GAO for being so critical of a draft proposal, and assured the GAO that "[i]ndeed, the process will not be complete until EPA circulates its draft to the public for comments and then releases a final product that is responsive to those comments." Assurances notwithstanding, some six weeks later the Administration finalized this deeply flawed proposal without any opportunity for public review or comment. This short-circuiting of the public comment process does not square with the principles of public right-to-know, or EPA's lip service in support of an open and transparent process.

Backlog at IRIS: Timeliness is already a terrible problem that cannot bear to be compounded by further delay

In the U.S., there are about 8,000 chemicals in commerce deemed "economically significant" (i.e., produced or imported at a rate greater than 10,000 pounds per site annually). Unfortunately, only about 550 chemicals in total have been evaluated in the IRIS program. Even when compared just to the universe of chemicals regulated by EPA, IRIS is obviously failing to adequately serve the public's needs. For instance, the EPA is responsible for regulating the emissions of 188 hazardous air pollutants (HAPs) under the Clean Air Act, but only 129 of them appear in the IRIS database. In other words, in almost 20 years since IRIS was created, the EPA has been unable to complete Toxicological Reviews for nearly one-third of these dangerous pollutants.

Furthermore, even when important chemicals are in the IRIS database, the risk assessments available for many of these chemicals are outdated: the average assessment on IRIS is over 13 years old, with the oldest having not been significantly revised since the mid-1980s. Considerable new evidence of toxicity has emerged for many of these chemicals since their last assessment, which renders the conclusions potentially obsolete and limits their usefulness and credibility with regulatory agencies.

According to the IRIS website, the program has finalized only thirteen assessments since 2004. As GAO notes "[t]he IRIS database is at serious risk of becoming obsolete because EPA has not been able to routinely complete timely, credible assessments or decrease its backlog of 70 ongoing assessments." [15]

Consider for example *Trichloroethylene* (TCE), a solvent used as a degreasing agent. TCE is one of the most common contaminants of Superfund sites across the nation, primarily from military uses, and is linked to cancer, including childhood cancer, and birth defects.[16] The IRIS draft was initiated a decade ago, in 1998. In 2001, EPA concluded that TCE was "highly likely" to cause cancer and specifically noted the added health risks when exposures took place during childhood. Finalization of that assessment has been held up after repeated objections from military contractors and the Department of Defense. Finally it was reviewed by the National Academies, which issued their report in July 2006, finding that the data linking TCE with cancer was even stronger than EPA IRIS staff had determined, and recommending that the IRIS assessment be finalized as soon as possible. Nonetheless, the Defense Department continued to insist that it not be finalized until more data was available, and today the assessment has still not been finalized and no target date for its completion has been set.[17]

Clearly, constructive reform for the IRIS program would focus on increasing resources available to undertake IRIS reviews as well as policy changes that would streamline the difficult decision-making inherent in the process. The new procedures run completely counter to these goals and will only exacerbate this backlog.

Delays to IRIS assessments result in continued unsafe exposures to humans and wildlife

Setting a health assessment standard under IRIS is only the first step in a long regulatory process. For example, for the EPA to establish a national drinking water standard, the Agency would typically reach out to stakeholders for input and perhaps even convene a Federal Advisory Committee, which could take over a year. Additionally, the docket for a proposed rule could remain open for at least a few months to collect comments from the public. Depending on the extent of the comments received, the Agency could again take up to a year or more to address and respond to those comments. In the end, it could take the Agency years, even decades, to finalize a drinking water regulation.

As new or updated IRIS assessments continue to languish, or get weakened to satisfy the demands of OMB and federal agencies including the Department of Defense and Department of Energy, the process of setting health standards becomes unspeakably prolonged. And the public continues to suffer due to lack of adequate public health protections.

For example, the administration has successfully blocked a much needed update of the IRIS assessment for formaldehyde. An updated assessment reflecting recent science that shows greater health hazards posed by formaldehyde could ultimately be the basis of establishing stricter emissions or exposure limits from building materials and other sources. Meanwhile, people living in temporary trailers provided by FEMA after hurricane Katrina have complained of a host of illnesses they believe are related to the high levels of formaldehyde which they have been exposed to in those trailers. At this time, the IRIS program estimates that it will finalize its assessment by the end of 2009.[18]

Similarly, delays with IRIS assessments has contributed to an inexcusable failure to develop a national health-protective standard for perchlorate, a component of rocket fuel and other explosives, in drinking water. Scientific evidence is overwhelming that exposure to perchlorate, an iodine uptake inhibitor in the thyroid gland, can cause significant development problems for developing infants. Subtle alterations of thyroid hormones during pregnancy – even within the normal range – have been associated with decreased intellectual and learning capacity in childhood.

Approximately 350 public water systems serving over 41 million have reported perchlorate detections.[19] The source of the contamination at many of these sites is defense and aerospace facilities and military installations. [20] The Defense Department mounted a years-long battle, and elicited White House support, against IRIS draft assessments in 1998 and in 2002 (both assessments were subject to public comment and external peer review) that had determined that even low doses of perchlorate may be harmful to early development of the human brain.[21] The final IRIS assessment was not completed until 2005.[22] Due to the year's-long delay in assessing and quantifying the harm posed by perchlorate in the IRIS program, the public remains years away from a national drinking water standard that will protect their health.

Objectivity and transparency of IRIS review is paramount

IRIS assessments must be shielded from political interference and be open to public scrutiny to ensure their scientific rigor and adherence to public health protective policies.

Under the new IRIS process, polluting federal agencies are provided excessive and redundant opportunities to intervene in the development of the IRIS assessments, shielded from scrutiny by the scientific community and the public. This is indefensible. The IRIS assessments and the comments provided by federal agencies, academics, industry, public interest groups, the general public, and others regarding drafts are supposed to be about science. The Administration has no reason for insisting upon secrecy other than to shield injection of politics and policy into the scientific debate, and avoid public airing of scientific arguments that won't stand up to public scrutiny.

Political appointees in the EPA undermine EPA's mandate to protect human health and the environment

The director of the IRIS program, George Gray, is clearly subverting the mission of the EPA in the development of the new IRIS process, essentially carrying out the mission of the OMB instead. Gray, who is EPA Assistant Administrator for the Office of Research and Development was previously the Director of the Harvard Center for Risk Analysis, a seemingly prestigious academic center but one quite notorious for its extensive support from corporate money and its tendency to promote industry perspectives in environmental health policy deliberations. With Gray holding direct management power over the IRIS program the Administration has ensured that EPA resistance to the agenda of undermining public health protections will be minimal, and, more often, will be aided by its political appointee.

A documented example of Gray's role in blocking the work of his own IRIS staff is the case of the Toxicological Review of tetrachloroethylene also known as perchloroethylene (perc), a dry cleaning and degreasing chemical and widespread groundwater contaminant. The IRIS assessment was initiated in 1998. In 2006 *Risk Policy Report* revealed that George Gray was insisting that his staff reanalyze the cancer risks of the chemical to try to fit the data to a model that would have assumed (without scientific evidence) that low doses were safe, whereas the staff's careful review of all available data did not support this assumption. [23] In addition, Gray's directive contradicts EPA's established, peer-reviewed cancer guidelines. Had the IRIS staff complied with Gray's directive, it would have resulted in a less-protective assessment. This assessment has still not been updated.[24]

In short, the political appointee currently in charge of the IRIS program, and defending the Administration's new reforms to Congress and the public, has blocked an updated assessment of a chemical polluting groundwater across the nation, and is insisting EPA scientists use unsupported and inadequately protective assumptions in a model intended to downplay the potential harm posed to the public by the chemical.

According to NRDC discussions with IRIS staff, additional instances of interference by George Gray to delay or weaken assessments include:

- blocking IRIS from posting acute (less than 24 hour) risk values.[25] Acute risk values are relevant to communities that are exposed to chemicals by burst releases of toxics (smokestacks, etc.) that may not exceed short-term (days-weeks) or long-term (months-years) regulatory standards, but may still pose a hazard to acutely exposed individuals.
- blocking IRIS from posting summaries of its assessments online, arguing that the summaries give a naïve public and regulators inaccurate impressions, contribute to misunderstandings, and are misused.

- blocking the IRIS staff recommendations to apply a 10-fold safety factor to site-specific assessments where children may be exposed to ethylene oxide, a potent human carcinogen with evidence that exposures during early life significantly increase the risk of developing cancer. Use of such a safety factor under precisely these conditions is specifically recommended in the *EPA Supplemental Cancer Guidelines on Children's Exposure*.

These examples should be alarming to any member of Congress, and any member of the public, who cares about ensuring that the best science is used by EPA to determine the risks posed by dangerous chemicals and who cares about fully informing the public about the risks posed by exposure to toxic chemicals . It also illustrates why NRDC and other environmental and public health groups, as well as the GAO, are so concerned about the changes to the IRIS process that will allow more of the decision-making to take place behind closed doors, where political appointees can make demands on career employees, without having to defend the merits of their scientific arguments (or the injection of policy and political preferences in a scientific process) before the public.

Conclusion

Properly implemented, the EPA IRIS program provides a critical scientific service to the public. Like other vital EPA programs, it must be preserved and protected so that EPA's scientists can conduct their work without political interference. The EPA's authority to determine the risks posed by hazardous chemicals should not be sacrificed to the desire of other federal agencies' or industry interests in avoiding clean-up costs or requirements for additional controls on emissions and exposures.

There are hundreds of potentially dangerous chemicals that are either already in the IRIS database but need to be updated, or that have not yet been added. Without an open, credible, effective, science-based, fully-funded program to develop these assessments without political interference from the White House or other federal agencies, EPA will continue to fall further behind in a fundamental program that serves as the foundation for fulfilling its mission: protecting the environment and public health.

As discussed above, the chemical industry has had great success, with the assistance of EPA's political appointees, in blocking, delaying or weakening individual health standards and undermining the fundamental program that establishes the level of risk posed by toxic chemicals. The third prong in industry's attack on environmental protections has been to attack the objectivity and credibility of independent and government scientists, while shamelessly promoting the supposed objectivity of industry scientists and consultants, many with direct financial conflicts in the matters they are reviewing. Sadly, EPA's political appointees have aided and abetted industry in this effort as well.

EPA'S MISUSE OF PEER REVIEW GUIDELINES TO DISMISS DR. RICE'S PEER REVIEW OF PBDEs IS A BLOW TO GOVERNMENT EXPERTS AND A PERVERSION OF THE GUIDELINES

When scientific experts were selected to peer review the EPA draft human health assessment for the polybrominated diphenyl ethers (PBDEs), a class of toxic flame retardants, there could be no better choice than Maine state toxicologist Dr. Deborah Rice to chair the peer review. She is an excellent scientist, respected among her peers, and even a recipient of a Level I Scientific and Technological Achievement Award (STAA) from EPA in 2004 for "exceptionally high-quality research" on lead toxicity.[26] Moreover, Dr. Rice is a public employee. Public servant scientists like her represent our most valuable brain trust of readily-available independent scientific expertise. Unlike experts for hire, government scientists have no financial stake in the outcome of a chemical review.

EPA opted to use an outside contractor to conduct the external peer review, which is a common practice. Deborah Rice was made chair of the peer review panel and submitted individual comments, as did the other panel members. However, a notice posted on the IRIS website states that EPA excluded Dr. Rice's comments from the final report *"due to the perception of a potential conflict of interest."*[27] (Italics added for emphasis).

The actions taken by the EPA to dismiss one of their most respected and credible scientific reviewers was in direct response to a written request from the Brominated Flame Retardant Industry Panel (BFRIP) of the American Chemistry Council – the manufacturers of PBDEs -- dated May 3, 2007, one week after the peer review workshop.[28] George Grey, EPA's Assistant Administrator for Research and

Development, referred directly to the letter, and a subsequent meeting with the ACC, when responding in writing to the BFRIP. Gray's letter states: "At the June 15 [2007] meeting, EPA listened to your concerns about a potential conflict of interest on the part of the Chairperson … Since then, we have decided that the Chairperson's comments would not be considered…and that the Chairperson's comments would be removed from the Final Report of the external peer review."[29]

EPA has not provided a rationale for its dismissal of Dr. Rice, except the website statement quoted above.[30] Clearly however there was no financial conflict. Moreover, Dr. Rice meets all the criteria of a knowledgeable, respected scientific expert.

In stark contrast, as Chairman Dingell and Congressman Stupak documented in their April 2, 2008 letter to EPA on this topic, there are no fewer than nine examples of industry scientists with blatant financial conflicts of interest who were never removed from EPA panels. Some of these people had also made public statements directly on the science they were adjudicating.

Moreover, on the same peer review panel that Dr. Rice had chaired, the Agency retained Richard J. Bull of MoBull Consulting as a peer reviewer, despite his sullied reputation for having failed to disclose relevant financial conflicts of interest on a prior committee of the National Academies National Research Council (NRC). In 2004, Richard Bull was asked to resign from the NRC committee reviewing the health hazards of the rocket fuel perchlorate after he failed to disclose that he was being paid by

Lockheed Martin to serve as their scientific expert in litigation.[31] Although the case was still ongoing at the time, Bull failed to reveal these direct financial conflicts to the NRC staff.[32] [33] The NRC asked Bull to resign from the committee.[34] The EPA leadership's hypocritical favoritism to industry consultants, while our own public servants are unfairly dismissed, rightfully makes the American public cynical about our federal agencies and their cozy relationship with polluters.

EPA made a serious error in judgment in disqualifying Dr. Rice from this panel. The EPA Peer Review Handbook recognizes that peer reviewers can hold strong opinions, noting as an example that, "as a final layer of review" the National Academies of Science "specifically recruit reviewers with strong opinions to test the scientific strength and balance of their reports."[35] Some scientific journal editors also do this with submitted manuscripts that could be controversial, with the goal of having the opportunity to respond to the full range of potential criticisms during the final draft stage of the document and thereby avoiding such criticisms after it is finalized.

The way George Gray has applied the peer review guidelines, an expert scientist like Deb Rice has a potential conflict – which is well-understood to mean a financial interest -- by taking a public position supporting phasing out the use of chemicals that are scientifically proven to be persistent, bioaccumulative, and toxic (PBTs) in cases where safer alternatives are readily available. This position is not in conflict with the science evidence, it is not in conflict with the scientific consensus among public health experts, and it is not in conflict with many state public health agencies where some PBDEs have been banned or restricted, including Washington, California, and Maine. [36] The only potential conflict that Dr. Rice may have is with the American Chemistry Council and their member companies that manufacture PBDE's; those groups continue to defend the chemical and testify against state bans.[37]

CONCLUSION

In his book, Doubt is Their Product: How Industry's Assault on Science Threatens Your Health, David Michaels emphasizes that the failures of EPA to regulate hazardous materials are not the fault of most agency scientists or career employees, "many of whom are heartsick that their work has been so undermined, to put it mildly, and that their once-proud agency has become just another enabler for the polluters and the poisoners."[38]

We appreciate the efforts of Congress, and this subcommittee, to investigate and oversee recent actions by the Administration including undermining the IRIS program and working in concert with industry to attack the integrity and independent of reputable government scientists. Congress needs to protect the public servants that are trying to do their jobs and serve the mission of the EPA, and prevent or overturn actions by Administration officials that weaken environmental and health protections for the public.

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Mr. STUPAK. Thank you.

Mr. Parshley, your testimony, please.

STATEMENT OF DAVID PARSHLEY, PROJECT MANAGER, GLYNN ENVIRONMENTAL COALITION

Mr. PARSHLEY. Good afternoon, Chairman Dingell, Chairman Stupak and members of the Committee. My name is Daniel Parshley. I am the Project Manager for the Glynn Environmental Coalition, a community nonprofit organization ensuring a clean environment and healthy economy for citizens of coastal Georgia.

The committee's February 5, 2008, letter to the Weinberg Group and its April 2, 2008, letter to the American Chemistry Council concerning the journal Regulatory Toxicology and Pharmacology was of great interest to the Glynn Environmental Coalition since this journal has been used to deny our community the basic protections that most Americans take for granted. Toxaphene, a now-banned pesticide composed of more than 670 chemicals, was manufactured in Brunswick, Georgia, by the Hercules Corporation from 1948 to 1980 and disposed of in many landfills and our estuaries. Now this toxic waste has spread throughout our community, including two Superfund sites, one of which, the Hercules 009 landfill, is located next to an elementary school. In 1991, EPA Region 4, the State of Georgia, and the Hercules Corporation, which manufactured the pesticide, met and agreed to use an analytical method that only reported a few of the toxaphene chemicals present. The EPA Office of Inspector General found this analytical method was inappropriate and that it did underreport the amount of chemicals present. The Inspector General ordered new and appropriate analytical methods be developed. The Inspector General was joined by other federal agencies including the Agency for Toxic Substance and Disease Registry and the Army Corps of Engineers.

In response, EPA Region 4 and the Georgia Environment Protection Division toxicologists published a paper in the journal Regulatory Toxicology and Pharmacology by Drs. Ted Simon and Randall Manning, advocating the reporting of only three of the 670 chemicals in the toxaphene mixture. The article did not present any new data but was rather a creative reinterpretation of existing scientific studies that came to a radically different conclusion about the toxic and carcinogenic properties of toxaphene. The Inspector General noted that the Simon and Manning method would underestimate the amount of toxaphene chemicals present and would exclude the toxaphene chemicals present in the largest amounts in our community. Furthermore, the Inspector General accepted the report under the condition that the authors produce the calculations used to reach the conclusions. Neither EPA Region 4 nor the authors have been able to produce the calculations. The Simon and Manning article has been extensively reviewed and commented upon by the Glynn Environmental Coalition and numerous outside biochemists and toxicologists who found deficiencies and inaccuracies in the journal article as well as the journal's bias toward industry.

Scientific standards require transparency and reproducibility. We believe that our community's needs are not being properly met by the EPA's reliance on such questionable science. Our request of

EPA Region 4 is very simple: test our elementary school and report all the chemicals present. For more than 10 years, the Glynn Environmental Coalition has asked EPA Region 4 to retest by an appropriate analytical method Altama Elementary School, which abuts the Hercules 009 Superfund site. We want all chemicals present to be tested for and appropriately reported. For more than 10 years, EPA has been unresponsive. Earlier this year, EPA Region 4 made a presentation to our board of education that used the Simon and Manning article from Regulatory Toxicology and Pharmacology to conclude that even if toxaphene was present on school property, the chemicals are not a health risk to elementary school children. There appears to be a scientific consensus in addition to a general consensus among federal agencies except EPA that the Simon and Manning method is inadequate to test for toxaphene. In addition, the Weinberg Group has been hired by Hercules to reassess toxaphene's toxicity. Tactics noted by the Committee in its February 5, 2008, letter have been put in motion including a scientific advisory panel to design two studies to determine the toxicity of only a few chemicals in the toxaphene mixture. We fear that there is a concerted effort by industry and EPA that is opposed to the appropriate testing of our community.

In closing, the Glynn Environmental Coalition is grateful for your attention to the abuses being perpetrated under the guide of science through the journal Regulatory Toxicology and Pharmacology and consulting firms such as the Weinberg Group. We have tried to briefly outline how EPA has delayed the proper testing of toxaphene in our community. I conclude by asking the simple question: do we ask too much when we ask that our elementary school be tested by an appropriate method and report all the chemicals present?

Thank you for allowing me to testify, and I look forward to answering any questions you might have.

[The prepared statement of Mr. Parshley follows:]

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September 18, 2008

Congressman John Dingell, Chairman
Committee on Energy and Commerce
316 Ford Office Building
Washington, DC 20515

Re: Testimony concerning the investigation into *Regulatory Toxicology and Pharmacology*, and impact of this publication on Brunswick, Georgia.

Honorable John Dingell,

The Committee's February 5, 2008 letter to the Weinberg Group and its April 2, 2008 letter to the American Chemistry Council concerning the journal *Regulatory Toxicology and Pharmacology* (RTP) was of great interest to the Glynn Environmental Coalition (GEC) since this journal has been used to deny our community basic protections that most Americans take for granted.

Summary

Our community has a very simple request of EPA Region 4: test areas contaminated by toxaphene pesticide and report all the chemicals present.

Toxaphene, a now banned pesticide, was manufactured in Brunswick, Georgia, from 1948 to 1980 and disposed of in several landfills, and in our estuary; now this toxic waste is spread throughout our community, including two Superfund Sites, one of which is located next to an elementary school. In 1991, the U.S. Environmental Protection Agency (EPA), the State of Georgia, and the Hercules Corporation, which manufactured the pesticide, met and agreed to change the analytical method for toxaphene to one that reported toxaphene and "some other product". Our Coalition's efforts resulted in the EPA Office of Inspector General (OIG) finding that the analytical method developed was inappropriate, and that it under-reported the amount of chemicals present; the OIG ordered a new and appropriate analytical method be developed. In response to the EPA OIG, EPA Region 4 and Georgia Environmental Protection Division published a paper in *Regulatory Toxicology and Pharmacology* advocating the reporting of only

3 of the 670+ chemicals in the toxaphene mixture. Even though the EPA OIG found the EPA Region 4 method would under-report the amount of chemicals present, EPA Region 4 has continued to advocate for methods that will either under-quantify or not report toxaphene chemicals present. The GEC asked EPA Region 4 to retest, by an appropriate analytical method, Altama Elementary School, which abuts a Superfund Site with toxaphene manufacturing wastes and has known releases to school property. Instead of testing by an appropriate method, EPA Region 4 did a presentation to the Board of Education that used the article from *Regulatory Toxicology and Pharmacology* to conclude that even if toxaphene was present on school property, the chemicals are not a human health risk.

Documents obtained from EPA Region 4 indicate that, in cooperation with Hercules Incorporated, efforts continue to develop and implement another analytical method that will only report a few of the chemicals present. We want appropriate testing conducted and all the chemicals present reported. Meanwhile, the risk to our school children and others exposed to toxaphene-contaminated soil, air, water, and seafood will remain undetermined.

Background and Discussion of Issues

Toxaphene, a now banned pesticide, was manufactured in our community from 1948 to 1980. Pesticide manufacturing wastes were disposed of in several landfills, estuary, and two Superfund Sites, one of which is located next to Altama Elementary School. Toxaphene migrated from the Hercules Plant site into surrounding neighborhoods, and from the Hercules 009 Landfill Superfund Site to Altama Elementary School. An estimated 2 to 3 million pound of toxaphene manufacturing wastes were released into the estuary.

In 1991, the U.S. Environmental Protection Agency (EPA), the State of Georgia, and Hercules met and agreed to change the analysis and quantification method for toxaphene to one that reported toxaphene and "some other product". The Toxaphene Task Force (TTF) was formed and was composed of chemists from EPA Region 4, Georgia Environmental Protection Division, and Hercules Incorporated. As a result of this change in how toxaphene was quantified by the TTF, none was reported when actually present above levels set to protect human health and the environment.[1] (Attachment A) When an analytical method fails to detect or report chemicals present, public health is jeopardized by the false belief that the seafood, soil, water, or sediments are safe to consume or to be exposed. Furthermore, the integrity of the nation's food basket is compromised when flawed analysis allows contaminated seafood to be harvested and sold.

The GEC brought our concerns about the under-quantification of toxaphene to the attention of EPA Region 4 throughout the 1990's without satisfactory results. The GEC submitted our concerns to the EPA OIG, which became a formal audit that culminated with the EPA OIG releasing *Appropriate testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (Report 2005-P-00022, September 26, 2005, Assignment 2004-124).

Dr. R. Kevin Pegg, in his capacity as our community's technical advisor under an EPA Technical Assistance Grant for the Hercules 009 Landfill Superfund Site, reviewed and commented upon the EPA OIG report.[2] (Attachment B) Dr. Pegg wrote an in-depth discussion of the toxaphene analysis and quantification issues covered by the EPA OIG, and the uncertainty caused by Toxaphene Task Force analytical method.

Simon and Manning - EPA Region 4 Response to the EPA Office of Inspector General

In response to the EPA OIG Report, EPA Region 4 and the State of Georgia produced the article, *Development of a reference dose for the persistent congeners of weathered toxaphene based on vivo and in vitro effects related to tumor promotion*, which was published in *Regulatory Toxicology and Pharmacology*, by Ted Simon, EPA Region 4; Randall Manning, Georgia Environmental Protection Division, hereafter referred to as Simon and Manning.[3] Noteworthy is that the article did not present any new data, but rather was a creative reinterpretation of existing scientific studies that came to a radically different conclusion about the toxicological properties of toxaphene, and advocated testing for only three of the 670+ chemicals in the toxaphene mixture, which would not be present or only in very small amounts. The EPA OIG found the article interesting but noted that the method proposed would underestimate the amount of toxaphene chemicals present, and would exclude the toxaphene chemicals present in the largest amounts. Furthermore, the OIG accepted the report under the condition that the authors produce the calculations used to reach the conclusions. Neither EPA Region 4 nor the authors have been able to produce the calculations used to reach the conclusion presented in the article.

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[1] Under Quantification of Polychlorinated Camphene (Toxaphene) in Brunswick, Glynn County, Georgia. January 2001. http://www.glynnenvironmental.org/ToxapheneAnalysis.htm

[2] EPA Toxaphene Testing Method Found Inappropriate, October 2005. http://www.glynnenvironmental.org/009TAR10-05.htm

[3] Ted Simon, T, R. Manning. Development of a reference dose for the persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion. Regulatory Toxicology and Pharmacology, Volume 44, Issue 3, April 2006, Pages 268-281

The Simon and Manning article published in *Regulatory Toxicology and Pharmacology* has been extensively commented upon by the GEC. [4] (Attachment C) Simon and Manning argued for using only three of the 670+ chemicals in the toxaphene pesticide mixture for quantification and human health risk analysis, which are referred to as p-26, p-50 and p-62 congeners (a congener is a single chemical from the toxaphene mixture). The premise of their reasoning was from a study of toxaphene in fish from the North Atlantic Ocean, Investigation into the Monitoring, Analysis and Toxicity of Toxaphene in Marine Foodstuffs study (MATT).[5] The MATT study selected the p-26, p-50 and p-62 congeners for analysis because it had previously been determined that they were the most prominent in the seafood from the area being studied. The prominent chlorinated camphene congeners in manufacturing wastes in Glynn County are very different, with Hx-Sed and Hp-Sed being the most prominent. Simon and Manning fails to conduct any analysis of what congeners are appropriate for areas contaminated by toxaphene manufacturing wastes.

The premise of the Simon and Manning article was fatally flawed for several reasons.

1. The selection of p-26, p-50 and p-62 congeners is used as an indicator of toxaphene in areas where they are the primary congeners, such as northern latitudes, and is inappropriate for southern latitudes such as Brunswick, Georgia. The primary analytical use of p-26, p-50 and p-62 congeners is as an indicator of toxaphene and not as a quantification or risk assessment tool.[6] The MATT study found relevance in the p-26, p-50 and p-62 congeners only because exposure is

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[4] Comment from the Glynn Environmental Coalition on the June 20, 2006, EPA Region 4, Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (Report 2005-P-00022, September 26, 2005); Assignment 2004-124. September 7, 2006. http://www.glynnenvironmental.org/009IG-comments-09-06.htm

[5] MATT, 2000. Final Report, Investigation into the Monitoring, Analysis and Toxicity of Toxaphene in Marine Foodstuffs FAIR CT PL.96.3131.

[6] Oetjen, K., H. Karl, Levels of toxaphene indicator compounds in fish meal, fish oil, and fish feed. Chemosphere. July, 1998.

exclusively from North Atlantic Ocean seafood exposed to atmospheric distilled chlorinated camphene, which results in higher percentages and ratios of the three congeners.

2. The range of p-26, p-50 and p-62 congeners vary widely in seafood so total chlorinated camphene, or total toxaphene, is measured for toxicological evaluations. The range of toxaphene congeners can range widely, but as a rule, the higher in the northern latitudes the seafood was obtained, the greater the percentage of p-26, p-50 and p-62 congeners. The use of p-26, p-50 and p-62 congeners is less useful as an indicator for seafood from southern latitudes. Total toxaphene is measured when a risk assessment is being conducted.[7] Tables 6 and 7 in the Simon and Manning paper demonstrate the significant decrease in p-26, p-50 and p-62 congeners in Glynn County, which has been noted in other studies.

3. The comparison of seafood exposed to dumped toxaphene manufacturing wastes versus atmospherically distilled chlorinated camphene is inappropriate. Simon and Manning violate the basic principles of scientific investigation by drawing conclusions between dissimilar data sets, and failed to report that the routes of exposure of the marine organisms in the data sets were vastly different. This omission invalidates all conclusions derived. The injection of so many variables, and the failure to report these variables, draws into questions the conclusions reached by Simon and Manning. A review of literature would have revealed that use of p-26, p-50 and p-62 congeners is inappropriate for southern latitudes.

4. Dioxin is a component of toxaphene manufacturing wastes and must be taken into consideration when planning sampling, analysis, and risk assessments. Simon and Manning ignore the known additional toxicological properties of toxaphene manufacturing wastes. Toxaphene manufacturing wastes contain their own unique composition of congeners, compounds, and contaminants that must be considered when evaluating risk to human health and the environment. The simplistic approach to toxaphene identification, quantification, and risk assessment presented by Simon and Manning will pose a significant threat to human health and the environment.

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[7] Chan, H. M., F. Yeboah. Total toxaphene and specific congeners in fish from the Yukon, Canada. Chemosphere. August 2000.

5. When p-26, p-50 and p-62 toxaphene congeners were measured in seafood from Brunswick, Georgia, they ranged from 1.56% to 8.69%, and the average was 4.80%. The p-26, p-50 and p-62 congeners are not the most prevalent in Brunswick, Georgia, and are inappropriate for use as chlorinated camphene indicators. The MATT study found the range of p-26, p-50 and p-62 toxaphene congeners in fish exposed via atmospherically distilled toxaphene in the Northern Atlantic Ocean ranged from 8.02% to 58.05%, and averaged 22.45%.

Dr. R. Kevin Pegg, in his capacity as our community's technical advisor under an EPA Technical Assistance Grant, reviewed and commented upon the Simon and Manning article and noted many deficiencies and scientific inaccuracies.[8] (Attachment D) Significant flaws were found in the conclusions concerning toxaphene's carcinogenic and genotoxic properties. Furthermore, it was noted that the authors generalized, speculated, and infer to such a degree that meaningful conclusions cannot be drawn.

Dr. Kathy Burns reviewed and commented upon the Simon and Manning article and found many scientific inaccuracies concerning the arguments presented concerning carcinogenicity and a lack of adherence to EPA policy and procedures.[9] (Attachment E)

Dr. Jennifer Sass, Natural Resource Defense Council, also provided comments concerning the Simon and Manning article and noted the bias of *Regulatory Toxicology and Pharmacology* towards industry perspectives, which was supported by 18 additional organizations knowledgeable about the issue. [10]

> It should be extremely concerning to taxpayers that a scientific article that proposes to disregard all but a handful of PCC congeners is co-authored by scientists from EPA Region 4 and the Georgia Environmental Protection Division (Simon and Manning, 2006). Though no source of funding is disclosed, it is published in a journal, *Regulatory Toxicology and Pharmacology*, well-known to be biased towards industry perspectives.

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[8] Review and Comments on the paper "Development of a Reference Dose for the Persistent Congeners of Weathered Toxaphene based on In Vivo and In Vitro Effects Related to Tumor Promotion" by Simon and Manning. August 2006. http://www.glynnenvironmental.org/ToxapheneAnalysis08-06.htm

[9] Comments on the Reliance of USEPA Region 4 on Simon and Manning, 2005 in Decisions Regarding the Hercules 009 Landfill Superfund Site in Brunswick, Georgia. September 7, 2006.

[10] Public Interest Comments on the Office of Inspector General Reports: Appropriate Testing and Timely Reporting are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia, Report 2005-P-00022; September 26, 2005. Report Report 2005-P-00022 (Addendum); September 13, 2005, and
More Information is Needed on Toxaphene Degradation Products, Report No. 2006-P-00007, December 16, 2005. October 2006. http://www.glynnenvironmental.org/009IG-comments-10-06.htm

> In fact, in 2002 the journal was targeted in a letter by over forty scientists, including noted international experts and journal editors, citing concerns about, "apparent conflicts of interest, lack of transparency, and the absence of editorial independence".[i] Specifically, their letter cites, "the journal's apparent bias in favor of industries that are subject to governmental health and environmental regulations". The letter goes on to identify financial supporters of the journal sponsor, including, the American Chemistry Council, Dow AgroSciences, R.J. Reynolds Tobacco Co., and others. Moreover, the letter identified a "significant percentage" of the editorial board with financial ties to companies whose products are the subjects of studies published in the journal. Is it any wonder, then, that this article advocating a weakening of cancer potency of toxaphene found its way to this journal? But, the fact that the authors are public employees suggests a concerning level of partnership between Hercules and the regulatory agencies.

All parties that reviewed and commented upon the Simon and Manning article found deficiencies and inaccuracies in the scientific argument presented.

EPA Region 4 Refusal to Report All Toxaphene Chemicals Present and Other Deficiencies

The EPA OIG noted in the audit closeout letter that EPA Region 4 remained steadfast in their refusal to test for and report all toxaphene chemicals present, and noted the calculations for the Simon and Manning article were not provided.[11] (Attachment G)

The EPA OIG's audit close-out letter was commented upon by Dr. R. Kevin Pegg. The lack of any supporting documentation for the Simon and Manning article was noted. (Attachment H)

The EPA Office of Inspector General made an error when asking for groundwater to be analyzed and risk assessed by the scheme presented in the Simon and Manning paper. Utilizing data from fish tissue, which metabolize and selectively bioaccumulate specific toxaphene chemical components, is inappropriate for soil, air, or groundwater. Furthermore, the OIG failed to recognize or address the source of contamination, which are toxaphene manufacturing wastes. Toxaphene manufacturing wastes contain additional contaminants such as dioxin that warrant consideration during testing and assessment of human health risks.

EPA Region 4 Refusal to Test Altama Elementary School

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[11] Memorandum: OIG Ombudsman Report 2005-P-00022, Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia. October 31, 2006.

After the EPA OIG found the method to test for toxaphene in our community inappropriate, the GEC requested that EPA Region 4 re-sample Altama Elementary School that abuts the Hercules 009 Landfill Superfund Site, which has documented releases to the school property from the Superfund Site and has only received testing by the method found to be inappropriate and known to under-quantify toxaphene. Further requests to test the school were made by the Glynn County Board of Education. Instead of testing the school, the EPA Region 4 made a presentation to the Board of Education on January 29, 2008. In this EPA Region 4 presentation, based upon the Simon and Manning article, the EPA concluded that even if chemicals were present, they were not harmful to the elementary school students, and refused to re-test a school known to be contaminated and only tested by an inappropriate method.

Both the GEC (Attachment I) and Dr. R. Kevin Pegg (Attachment J) commented on the January 29, 2008, EPA Region 4 presentation to the Board of Education and provided comments and examples specific inaccuracies to the school system's attorney.

EPA Region 4 Implementation of Simon and Manning Risk Assessment Method Instead of the EPA Integrated Risk Information System (IRIS)

According to EPA Region 4 documents, the Simon and Manning risk assessment scheme has been used to the exclusion of the body of scientific knowledge and the EPA IRIS database to rewrite documents for Superfund Sites contaminated with toxaphene. After the EPA Office of Inspector General October 31, 2006, close-out letter was received by EPA Region 4; efforts were made to implement the Simon and Manning risk assessment method at Superfund sites. The Terry Creek Dredge Spoils National Priorities List (NPL) Site Remedial Investigation/Feasibility Study documents were identified for revision to reflect the risk assessment scheme presented in Simon and Manning instead of using the EPA Integrated Risk Information System (IRIS) established for this purpose. [12] EPA Region 4 defined the best available science as Simon and Manning for toxicity. The next step identified was for the EPA Technical Services Section to develop Remedial Goal Options for soil and sediment based upon the risk assessment scheme in Simon and Manning. [13] The EPA IRIS database has been effectively been eliminated by EPA Region 4 as the risk assessment tool for toxaphene contaminated sites in Brunswick, Georgia.

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[12] EPA Region 4 Briefing Summary, Terry Creek Dredge Spoils, Brunswick, Georgia. July 31, 2007

[13] EPA Region 4, Path Forward, Terry Creek Dredge Spoils, Brunswick, Georgia. August 13, 2007

EPA Region 4 Implementation of the Hercules Analytical Method Instead of EPA Office of Inspector General Ordered EPA Office of Solid Waste Method

As the EPA Office of Inspector General (OIG) noted, EPA Region 4 resisted testing for and identifying all toxaphene chemicals, and advocated for reporting only the three toxaphene chemicals identified by Simon and Manning. EPA Region 4 noted that the national effort to incorporate the Gas Chromatography-Negative Ion Mass Spectroscopy (GC-NIMS) into SW-846, ordered by the OIG, is on a separate path and inconsistent with the Hercules method. Still, one of EPA Region 4's next steps was to prioritize their laboratory workload to incorporate the ability to perform Hercules' GC-NIMS.[14] This action strongly implies that EPA Region 4 was working in conjunction with Hercules to implement an analytical method other than the OIG ordered method under development by EPA Office of Solid Waste.

EPA Region 4 and Hercules Meet with EPA Office of Solid Waste to Advocate for Limited Toxaphene Chemicals Testing

On February 19, 2008, EPA Region 4 met with Shen-Yi Yang, of the EPA Office of Solid Waste, Arlington, Virginia, who is developing a formalized GC-NIMS toxaphene analysis and quantification method as the EPA OIG instructed. At this meeting, EPA Region 4 inappropriately pressured Ms. Yang to change the analytical method under development to one that would only measure the three chemicals identified in the Simon and Manning paper, which the EPA OIG already found to be a method that would under-report the amounts of chemicals present, and specifically exclude the chemicals present in the largest quantities (personal communication).

EPA Region 4 Information Withheld

Information has not been forthcoming from EPA Region 4. An effort was made to obtain additional information through a Freedom of Information Act request, but EPA Region 4 is withholding ~400 documents from 2006 forward that would shed further light on how the Simon and Manning article is being used, and on the Weinberg Group re-assessment of the toxicity of toxaphene.

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[14] EPA Region 4, Path Forward, Terry Creek Dredge Spoils, Brunswick, Georgia. August 13, 2007

The Weinberg Group Hired by Hercules to Perform Toxicological Studies on Toxaphene

The Weinberg Group was hired by Hercules to re-assess toxaphene's toxicity. Tactics noted by the Committee have been put in motion, including a Scientific Advisory Panel to design two studies. According to EPA documents, the first study will be used to design the second study to determine toxicity of only a few chemicals in the toxaphene mixture. Included on this panel is Dr. James Klaunig, a person of interest to the House Energy and Commerce Committee for his past activities. The comments of the Scientific Advisory Panel were incorporated into the testing plan, according to the August 21, 2007, presentation by the Weinberg Group.[15] Notable is that only a few of the chemicals from the toxaphene mixture will be used in the risk assessment.

In closing, The Glynn Environmental Coalition is grateful for your attention to the abuses being perpetrated under the guise of science through the journal *Regulatory Toxicology and Pharmacology*. We have tried to briefly outline how this journal has been used to argue for continued biased analysis and quantification of toxaphene in our community. Do we ask too much when we ask for our elementary school, and other areas tested by the method the EPA OIG found inappropriate, to be tested by an appropriate method and all the chemicals present be reported? Until appropriate testing is conducted, and all chemicals present are reported, toxicologists and health professional will not be able to assess the risk nor make recommendations to protect human health and the environment.

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[15] Toxaphene Risk Assessment: Re-evaluation and Data Development, James C. Lamb, Ph.D., DABT, FATS. The Weinberg Group Inc. Washington, DC. August 21, 2007.

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[i] Axelson O, Balbus JM, Castleman B, Cohen G, Davis D, Donnay A, Doolittle R, Duran BM, Egilman D, Epstein SS, Goldman L, Grandjean P, Hansen ES, Heltne P, Huff J, Infante P, Jacobson MF, Joshi TK, Ladou J, Landrigan PJ, Lee PR, Lockwood AH, MacGregor G, Melnick R, Messing K, Needleman H, Ozonoff D, Ravanesi B, Richter ED, Sass J, Schubert D, Sharpe VA, Socha A, Suzuki D, Teitelbaum D, Temple NJ, Terracini B, Thompson A, Tickner J, Tomatis L, Upton AC, Wyatt RM, Wigmore D, Wilson T, Wing SB. Letter to Academic Press and Elsevier Sciences, Inc. Re: Regulatory Toxicology and Pharmacology. November 19, 2002.

Attachment A

Under-Quantification of Polychlorinated Camphene (Toxaphene) in Brunswick, Glynn County, Georgia.

January 2001

Summary

The U.S. EPA, Georgia EPD, and Hercules Inc. met as the "Toxaphene Task Force" (TTF) and developed a method for identifying and quantifying the pesticide toxaphene in Brunswick, Georgia. The TTF method has threatened human health by failing to detect or significantly under quantifying toxaphene levels present in the environment. U. S. EPA and the Agency for Toxic Substance and Disease Registry toxicologist have documented why the TTF method fails to produce data that is useful in making their decisions and recommendations to protect human health. Analysis for toxaphene by gas chromatography with electron capture negative ionization mass spectrometric detection (GC-ECD and GC-ECNI-MS) has produced the data needed for toxicologist to make decisions protective of human health.

Background

The Glynn Environmental Coalition (GEC) is located in Brunswick, Glynn County, Georgia, where an insecticide mixture of polychlorinated camphene (PCC), commonly called toxaphene, was manufactured by Hercules Incorporated. Manufacturing of PCC took place at Hercules Incorporated, Brunswick, Georgia, from 1948 to 1980.[1] PCC is defined as camphene with 67% to 69% chlorine by weight, and is a complex mixture of over 670 separate chemicals. [2],[3],[4] During the period PCC was manufactured, PCC manufacturing wastes and PCC was discharged into the estuary by way of Dupree and Terry Creek at a rate of 250 to 300 pounds of PCC per day.[5] Fugitive emissions of PCC contaminated wind-blown dust, water runoff, and vehicle traffic distributed PCC throughout the neighborhoods around the Hercules Plant site. [6] In addition, significant amounts of PCC were deposited into at least four landfills and dumps in Glynn County.[7], [8]

In 1991, chemists from the EPA, EPD, and Hercules Inc., performed a limited study and developed a set of guiding principles for the determination of PCC in groundwater, soil, and manufacturing waste sludge samples from the Brunswick, Georgia, area.[9], [10] The results of this limited study was the development of the "Toxaphene Task Force" (TTF) methodology for the identification and quantification of PCC. The TTF methodology was further modified in

August 1997.[11] Even though the August 1997 modifications were proposed for only specified areas and only for soil and groundwater, the method has been used at Sites throughout Glynn County and has been used to determine PCC's in fish tissue for human health determinations.[12] The August 1997 method is also referred to as the "Hercules Protocol".[13]

The ability of the agreed upon TTF method to accurately identify and quantify PCC has been questioned by the Agency for Toxic Substance and Disease Registry (ATSDR) and the EPA.

Statement of the Problem

The method developed by the TTF for the identification and quantification of PCC in Brunswick, Georgia, seriously underestimates the true amount present, and excludes the PCC chemicals that health officials are most concerned about. Specifically, the TTF method fails to report the "total toxaphene" and "apparent toxaphene" that are the basis of recommendations by the EPA, Food and Drug Administration (FDA), and ATSDR toxicologist to protect human health and establish cleanup levels at PCC contaminated sites.

Local, State and Federal health officials rely upon the accuracy of data gathered on PCC levels to make recommendations to minimize or eliminate exposure of citizens through consumption of contaminated seafood, water, or contact with contaminated soil, sediments, and sludge. Based on PCC data collected, interim actions are recommended to protect the public in the form of seafood consumption advisories, and emergency removal actions, while long-term remedies are developed. High quality and accurate data is crucial in taking short-term actions and recommendations, and developing long term remedial plans.

Health officials from the EPA and ATSDR have identified the TTF method as seriously flawed in providing data meaningful to their deliberations on the potential health ramifications from the consumption of PCC contaminated seafood, and exposure to PCC contaminated air, soil, sludge, sediments, and water. The EPA and ATSDR are specific in the type and quality of data needed to make decisions protective of human health and the environment. Likewise, the EPA and ATSDR have been specific in the ways the TTF method has threatened human health by failing to detect and understating actual PCC levels present. Most notable is that the TTF method excludes the fraction of the 670+ PCC chemicals that are of concern in making health based recommendations. Recent re-analysis of samples has shown that the TTF method failed to identify the presence of PCC in seafood at levels 52 times the EPA "do not eat" recommendation. The TTF method has failed to accurately identify PCC in many other samples, or to significantly understate actual levels of PCC present.

Discussion

Formation of the Toxaphene Task Force began at meeting on September 30, 1991, at the Georgia EPD. It was agreed that previously the regulatory agencies and Hercules had used a procedure that identified "apparent toxaphene" when analyzing environmental samples.[14] Analysis for "apparent toxaphene" is the criteria used by the U.S. Food and Drug Administration (FDA) to make health based recommendations for maximum levels of PCC in food.[15] It was agreed that if the U.S. EPA, Georgia EPD, and Hercules agreed upon the method and the findings of the task force, it would be used by the EPA for any work relating to the Superfund Site[16] or any RCRA matters pertaining to the Hercules facility involving toxaphene. It was proposed that those in attendance meet again to review the work of the task force and to discuss whether the samples do, in fact, reflect toxaphene or some other product. Clearly, a decision was made at the meeting to develop a PCC analytical method different from the health-based method currently in use.

The report of TTF, released June 4, 1993, was described as a very limited study of toxaphene analysis of real samples collected at the Hercules facility in Brunswick, Georgia.[17] The TTF method was designed to identify and quantify "technical toxaphene", instead of the "total toxaphene" or "apparent toxaphene" used by toxicologist in determining the potential risk to human health and the environment.

The TTF made specific changes in the identification and quantification of PCC that result in a significant reduction of "total toxaphene" and "apparent toxaphene". Quantification was limited to the 4-6 major peaks on the "back half" of the toxaphene chromatogram while many of the prominent PCC's found in the "front half" are associated with unmodified technical toxaphene.[18],[19],[20],[21] The TTF further excluded PCC from the quantification process by eliminating any peak which is larger in proportion to the other component peaks in the sample than in the toxaphene standard.[22] The U.S. Food and Drug Administration, in the "apparent toxaphene" method, instructs to include all peaks, and notes that relative heights and widths of matching peaks in the residue and reference standard will probably differ. [23]

One chemist from the U.S. EPA noted that the "latter peaks" in samples were decreased and the "early peaks" were increased in environmental samples from Brunswick, and that the TTF method may seriously underestimate the true concentration of toxaphene.[24],[25] Because early and disproportionate peaks are eliminated from the quantification in the TTF method, it produces much lower PCC quantification results than those found using the U.S EPA approved Contract Laboratory Program (CLP) analytical method. The U.S. EPA Region 4 Environmental Services Division Laboratory analyzed split samples by the TTF method and a contracted laboratory by the U.S. EPA approved CLP method. Results showed that the TTF method either failed to detect PCC or only identified as little as 3.2% of the PCC present.[26]

Seafood samples collected in 1997 by the Georgia Department of Natural Resources, and analyzed by the Georgia Environmental Protection Division using the TTF method, were re-analyzed by the Skidaway Institute.[27] While PCC was not detected in any sample (n=56) using the TTF method, Skidaway detected PCC in every sample up to 26 parts per million (PPM). Even when the EPA "do not eat" levels of 0.5 PPM was exceeded by 52 times, PCC was reported as "not detectable" in fish by the TTF method.[28] The Food and Drug Administration (FDA) has a maximum allowable PCC level of 5 PPM in commercially caught seafood sold in the United States, until revoked in 1993.[29] In addition, in setting the FDA level, it makes the assumption that the seafood will be diluted in the Nation's food basket. The FDA also explicitly states that FDA maximum allowable levels are not to be applied to a seafood source consumed by the local population. The TTF method failed to find PCC at over five-times the FDA commercial level, yet commercial seafood harvest continues within the areas. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), food tolerance restrictions for toxaphene (PCC) range from 0.1 to 7 ppm. Therefore, the failure of the TTF method to detect toxaphene at levels meaningful to the protection of human health and the environment presents local health threats and may have national significance.

ATSDR evaluated the data produced by the TTF method and found many concerns over it use.[30] The TTF method failed to accurately identify and quantify a known amount of the PCC in the calibration standard. They found that the composition of the weathered PCC in fish differs from that in the technical-grade PCC, and the PCC adsorbed on soil may have a different bioavailability than technical-grade PCC. In addition, the TTF method seems to eliminate the option to conduct a total area method that estimates the PCC concentration from all peaks in the chromatogram.[31] The ATSDR concluded that the use of the "back half" peak method (TTF method) is likely to result in significant underestimation of PCC concentration, and the estimated dose could be 10 times higher if historical data are taken into account for dose estimation.[32] ATSDR recommended that sensitive and specific methods, such as electron capture negative ion mass spectrometry (GC-ECNIMS) be used for the evaluation of toxaphene in fish and sediment.

Local, State, and Federal health officials depend on PCC data from the EPA, EPD, and Hercules Incorporated, in preparing remedial plans and making recommendations to potentially exposed citizens around contaminated areas. In addition, the Georgia EPD will NOT make a consumption recommendation without data.[33] An analytical method that fails to find the chemical of concern or that seriously understates the actual levels present fails to protect human health. Bad data leads to bad decisions and recommendations by local, State, and Federal officials that result in health threatening exposure of the citizenry. The integrity of the Nations food basket is compromised by flawed analysis that allows contaminated seafood to be harvested and sold.

Corrective action plans required by the EPA and EPD are promulgated on protection of human health and the environment. Remedial actions that are based upon faulty or inaccurate data will fail to fulfill the intent of the law, which is to protect human health. Any analytical method that fails to find the chemical(s) of concern (COC) at levels meaningful to the protection of public health is a threat to public health. When a method is represented to be accurate at levels meaningful to public health and fails to detect COC's, and the COC is reported as not present, public health is jeopardized by the false belief that the seafood, soil, water, or sediments are safe to consume or be exposed.

Conclusions

The Glynn Environmental Coalition (GEC) believes that the U.S. EPA, Georgia EPD, and Hercules have entered into an agreement that failed to identify and under reported PCC levels present. This agreement has led to data that is a threat to human health and the environment because health agencies are making seafood consumption and soil, sediment, and sludge exposure recommendations based upon flawed data. In addition, remedial actions by the U.S. EPA and Georgia EPD will not be protective of human health and the environment because cleanup levels will not accurately reflect true levels of PCC present.

Recommendations

The GEC is seeking the following remedy for PCC sampling that has not produced data meaningful to the protection human health .

1.) Order that all future PCC analysis and quantification be done using Gas Chromatography with Electron Capture and Electron Capture Negative Ionization Mass Spectrometric Detection (GC-ECD and GC-ECNI-MS) for environmental samples such as fin- and shellfish or other biota, soil, sediment, sludge, and water.

2.) Order that all analysis and quantification report "total" PCC levels present.

3.) Order sampling, analysis, and quantification of PCC by GC-ECNI-MS in all areas and media previously analyzed and quantified by the TTF method in Brunswick, Glynn County, Georgia.

Prepared by Daniel Parshley, Project Manager

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Attachment B

EPA Toxaphene Testing Method Found Inappropriate

Overview

The Environmental Protection Agency's Office of Inspector General recently issued a report entitled "Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia" dated September 26, 2005. This document, developed by EPA's Ombudsman, refutes Region 4 EPA's methods for analyzing toxaphene at the 009 Superfund Site and the Terry Creek Disposal Superfund Site, and at other areas around Glynn County, Georgia. Nearly 15 years of data collected on soil, air, water and biological samples tested in Brunswick are now in doubt.

Each department in the United Sates administration has an Inspector General office to provide oversight for the agency. Several years ago the Glynn Environmental Coalition formally requested an investigation on items ranging from toxaphene testing in Glynn County to questions regarding lack of compliance in the cleanups in Brunswick. This first report mainly investigates the issue of toxaphene analysis. The Office of Inspector General has concluded that the methods used by Region 4 have not and could not precisely determine the form of toxaphene found in Glynn County.

Background

The 009 Superfund Site is a former road construction borrow pit refilled with waste from pesticide manufacturing at Hercules Inc. Toxic sludge, off-grade product, and contaminated soil were deposited into the pit, some of which was below the water table at least part of the year. Although the Record of Decision—the legally mandated cleanup goals for the site--stated that all contaminated soils above 76 parts per million (ppm) would be stabilized *in situ*, the EPA allowed a much simpler cleanup of merely covering the waste with a soil/cement mixture using above-ground mixing techniques. At question are the legalities of changing cleanup plans without seeking community input, and whether or not the cleanup achieved any of the goals of the original Record of Decision.

The Terry Creek Disposal area is a marshy region at the confluence of Terry and Dupree Creeks in Glynn County that receives industrial runoff from the Hercules plant. Decades of dumping into the creek system and a series of dredging operations widely distributed toxaphene within the marshes. The main issue at this site is if toxaphene is accurately measured in seafood since the area is part of the local fishery.

In addition to the EPA regulated sites, "toxaphene-like" substances were found in the soils of local public schools and other public and private properties. Based on this Report by the EPA Ombudsman, these "toxaphene-like" materials are toxaphene congeners subject to EPA regulation. Overall, there is the major question of whether or not the EPA permitted testing giving false data on toxaphene. There are many scientific studies showing toxaphene can be measured more accurately than the techniques used by EPA in Glynn County.

Toxaphene and its breakdown products are poisons, mutagens, possible cancer agents and they do bioaccumulate.

Toxaphene

Internationally recognized scientific studies show there are usually three different types of toxaphene: technical, weathered and biological. Technical toxaphene is the type made at the factory and sold worldwide for agricultural pest control. Technical toxaphene is not one chemical, it is a mixture of about 200 different chemicals produced by adding chlorine to camphene, a chemical made from tree resin. Different manufacturing processes produce slightly different mixtures. Although the chlorination of camphene can produce any of about 600+ different chemicals (called congeners) most technical grades have about 200 chemical congeners. Weathered toxaphene occurs after toxaphene is used. Environmental processes such as air drying, sunlight and bacteria degrade toxaphene. Since each of the more than 200 chemicals in technical toxaphene breaks down differently, weathered toxaphene varies in the types of chemicals present. Some chemicals appearing in weathered toxaphene are not found in the original technical grade of toxaphene, but they are still some of the 600+ different types of chlorinated camphenes, they are just produced from technical toxaphene by environmental processes. Biological toxaphene occurs when plants and animals absorb toxaphene from the environment. Every bacteria, plant, or animal has a different ability to absorb toxaphene congeners. Fish tissues have a different set of toxaphene chemicals from humans. Some toxaphene congeners are found often and in high concentrations (a process known as bioaccumulation), other congeners rarely occur in animal tissues. Biological toxaphene is very different from technical toxaphene, but all of the compounds found in biological toxaphene are still members of the same set of 600+ congeners found in toxaphene.

Note that Glynn County, Georgia has a fourth and fifth type of toxaphene. Off-grade product, material that was not toxic enough to sell, and residue from manufacturing, were dumped locally both in the 009 landfill and into Terry Creek. This material was not the same as technical toxaphene, but was still toxic, mutagenic and potentially carcinogenic. It is only found near the sites of manufacture, such as Brunswick, Georgia. Off-grade product toxaphene and manufacturing residue toxaphene will still weather and bioaccumulate, just like technical toxaphene.

Types of toxaphene measurements

All of the methods for analyzing toxaphene use gas chromatography or "GC." GC separates all 600+ possible toxaphene compounds so that they can be seen and measured. There are several different measurement methods and technologies.

Total Area Method

This is the basic method required by the US EPA for chemicals with multiple congeners. It detects technical, weathered and biological grades of toxaphene, as well as the off-grade product and manufacturing residue forms. Basically, all of the possible toxaphene chemicals are detected and added together to quantify total toxaphene. This method was not used by the EPA in Brunswick, Georgia, but is used at other EPA sites in the United States and by other governments and researchers around the world.

Toxaphene Task Force Method

This method was developed by EPA Region 4 in Atlanta, Georgia, with Hercules Inc., and the State of Georgia. While gas chromatography is still used, only a few of the chemicals specific for technical toxaphene are used in the analysis. Even if other toxaphene chemical congeners are present, they are ignored. The toxaphene task force method (known as EPA Method 8081) detects technical grade toxaphene as well as the total area method; however 8081 does not detect all off-grade products, does not detect some forms of manufacturing residue toxaphene, and can only detect weathered toxaphene in the first few years after placing in the environment. The TTF method does not detect toxaphene after it has been in the environment for several years, and it does not detect biological toxaphene. The TTF method is apparently used only in Glynn County Georgia and nowhere else in the world. The method is not recognized by other governments or by researchers as a useful method because it under-reports the actual toxaphene concentration.

GC negative ion mass spectroscopy

This technique, called the NIMS method, can detect all forms of toxaphene and is a widely respected method with a high degree of scientific merit regarding interpretation of results. It is especially useful for detecting biological forms of toxaphene accumulation. This is the method favored by the EPA Inspector General. NIMS is still not approved by the EPA.

Discussion

Quoting from page 5 of the Ombudsman's report section titled **"EPA's Method Fails to Identify Toxaphene Breakdown Products in Groundwater"**: *"... the groundwater monitoring data collected at the site, using EPA's method, only identified the original toxaphene mixture in the groundwater."* Further, same page: *"When the OIG looked at the groundwater monitoring data for evidence of toxaphene breakdown products, the OIG found some evidence suggesting toxaphene breakdown products may be in the groundwater surrounding the Hercules 009 Landfill Site."*

In Appendix A of the report the OIG shows by example chromatograms and states, in the section titled **"EPA Method 8081 Does Not Identify Toxaphene Degradation Products"**: *"...EPA Method 8081 fails to detect toxaphene degradation products (i.e., "weathered" toxaphene or individual toxaphene congeners) in environmental samples."* Method 8081 is the method produced by Region 4 EPA's Toxaphene Task Force using the subset of toxaphene congeners.

The Ombudsman report also notes that EPA is required to monitor toxaphene degradation products. On page 21 in the section titled **"Superfund's Remedy Requires the Evaluation of Toxic Degradation Products"**: *"Therefore, the Superfund's MNA [Monitored Natural Attenuation] guidance requires EPA to anticipate and to test for the presence of potentially toxic degradation products at hazardous waste sites. Since toxaphene is known to degrade in the environment and these degradation products are thought to be toxic, EPA must evaluate the groundwater at the Hercules 009 Landfill site for toxaphene's degradation products..."*

The Ombudsman report noted other problems with the conduct of sampling by the EPA in Brunswick. An addendum to the report discussed potential problems with the cleanup of environmental samples using sulfur, and a second problem with heat settings on the instrument. Sulfur can interfere with the analysis, some instrument temperature settings fail to detect toxaphene. In combination with the inability of methods used by EPA to quantify weathered toxaphene, the potential biases of the cleanup and column temperature means that much of the data used by EPA to design and verify Superfund cleanups are doubtful.

The Report also cites comprehensive toxicology and body burden studies on toxaphene congeners conducted at a variety of laboratories. Notable among these is the MATT study (Investigation into the Monitoring, Analysis and Toxicity of Toxaphene in Marine Foodstuffs, 2000) describing the bioaccumulation of specific toxaphene environmental end-products in commercial fish species. EPA Region 4 should have been aware of these studies—it is their responsibility to follow the scientific literature. Region 4 should have responded to the growing body of literature regarding toxaphene years ago. In addition to criticizing toxaphene analysis the OIG report also faults EPA on lack of timely reporting, failure to make key decisions, and notes unacceptable modifications to "independent" third-party reviews before release to the public.

Concluding Remarks

For more than a decade EPA Region 4 used the toxaphene task force method (EPA Method 8081) in Glynn County despite research showing the method does not give valid data on environmental toxaphene. At this point it is not clear if cleanups at the 009 landfill and Terry Creek Outfall meet the legal remediation goals. It is not clear because EPA has used an unreliable method that cannot measure the types of toxaphene found in water and soil.

It is fair to say much of the data on toxaphene occurrence and exposure is "inconclusive" for samples taken in Brunswick and tested by method 8081. Not all of the thousands of samples examined so far are in error—obviously many observed both technical toxaphene and some forms of weathered toxaphene. However, virtually all of the groundwater and soil samples need retesting to verify the presence or absence of weathered toxaphene.

EPA is proposing developing new methods using the NIMS method advocated by the Inspector General. While there may be some debate over methods, one thing is crystal clear: EPA Region 4 should not be the agency to produce and validate any new toxaphene method. The Atlanta, Georgia EPA office is far too biased to be trusted with developing toxaphene methods.

Written by R. Kevin Pegg, Ph.D.; edited by Dr. Mary S. Saunders. Copies of the newsletter are available from the GEC, at the Glynn County library, or at **www.enviro-issues.net** on the Internet.

HERCULES LANDFILL SUPERFUND SITE
TECHNICAL ASSISTANCE REPORT
"This project has been funded wholly or partly by the U.S. Environmental Protection Agency under Assistance Agreement Number V994050-92-0 to The Glynn Environmental Coalition, Inc. The contents of this document do not necessarily reflect the views and policies of the U.S. Environmental Protection agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use."
Volume 14, Number 1, October 2005

Attachment C

September 7, 2006

Glynn Environmental Coalition
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Paul D. McKechnie, Director Public Liaison/Acting Ombudsman
U.S. EPA, Office of Inspector General
Office of Congressional and Public Liaison
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Boston, Massachusetts 02114-2023

Re: Comment from the Glynn Environmental Coalition on the June 20, 2006, EPA Region 4, Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (Report 2005-P-00022, September 26, 2005); Assignment 2004-124.

Mr. McKechnie,

Enclosed, please find comments from the Glynn Environmental Coalition (GEC) on the June 20, 2006, Environmental Protection Agency (EPA) Region 4, Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (Report 2005-P-00022, September 26, 2005); Assignment 2004-124. We trust the EPA Office of Inspector General will take the following comments into consideration in formulating the final OIG response to EPA Region 4.

The enclosed comments include reviews of the EPA Region 4 Response by R. Kevin Pegg, Ph.D., and Kathleen Burns Ph.D., and are included in the GEC comments by reference.

Sincerely,

Bill Owens, President

CC: Chris Baughman

Enclosures

Comments from the Glynn Environmental Coalition on the June 20, 2006, Environmental Protection Agency Region 4, Final Response to the Recommendations and Final Report for

the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (Report 2005-P-00022, September 26, 2005)

September 7, 2006

1. The OIG identified under quantification of chlorinated camphene as a problem at the Hercules 009 Landfill Superfund Site, and numerous other sites across the nation. Even when chlorinated camphene was present, the TTF method either reported none present or only quantified a small amount of the chlorinated camphene compounds indicated by the chromatogram. The question that MUST be answered is, "Will all chlorinated camphene present in environmental samples be identified and quantified?
Environmental sampling and analysis data is used to protect human health and the environment, and the same data will be used by several different scientific disciplines. Toxicologist produce health and risk assessments, biologists evaluate environmental risk to micro to macro biota, and remedial plans are developed to protect human health and natural resources. At a minimum, all chlorinated camphene MUST be reported in environmental samples. Neither the OIG nor the EPA Region 4 Response evaluated their recommendations and conclusions against the scientific disciplines that will be utilizing the data set from sites contaminated by chlorinated camphene or toxaphene manufacturing wastes.

2. The EPA Region 4, Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report (Response) *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (OIG Audit) constitutes a refusal to implement the recommendations in the OIG Audit, and misrepresents the finding of the OIG.
In the OIG Audit, specific recommendations were made for the quantification of chlorinated camphene.

> *"The OIG believes that spiked sample recoveries of the individual toxaphene congeners of interest, such as Hx-Sed, Hp-Sed, p26, p50, and p62, should be incorporated into any NIMS method considered by the EPA for developing and validating."*
>
> *"EPA needs to use a congener-specific analytical method (e.g., GC/NIMS) to positively identify and quantify toxaphene degradation products in the environment. The OIG highly recommends standardizing and validating the GC/NIMS method and inserting a EPA GC/NIMS method into SW-846."*

Contrary to the OIG Audit recommendations, EPA Region 4 has proposed chlorinated camphene quantification and risk assessments be based solely on p-26, p-50 and p-62 congeners and that all other compounds be excluded from the quantification and risk assessment process. As the OIG noted, Hx-Sep and Hp-Sed congeners account for the majority of chlorinated camphene found in Glynn County, Georgia. Even though the OIG identified the need for more toxicological data on the Hx-Sep and Hp-Sed congeners, EPA Region 4 has proposed elimination of these from the quantification and risk assessment process without presenting data in support of this conclusion. To the contrary, Hx-Sep and Hp-Sed congeners are the most prominent and represent a significant risk to citizens of Glynn County due to the chronic exposure via seafood, soil, and air.

The OIG noted that there are deficiencies in the studies used to determine the toxicity of chlorinated camphene, in that the exposure periods were short and did not represent the extended period of exposure (1948 to 2006) of those living in Glynn County. Further complicating the reaching of any conclusions is the lack of data about the chronic exposure to metabolites produced during human elimination of chlorinated camphene over the duration of exposure experienced in Glynn County, which is where chlorinated camphene was manufactured from 1948 to 1980. In addition, the majority of the data relied upon by the OIG and EPA Region 4 was from populations and food stuffs that derived chlorinated camphene levels from atmospherically distilled chlorinated camphene, which does not contain the same ratio of congeners as in Glynn County. Atmospherically distilled chlorinated camphene is very different than Glynn County where manufacturing wastes, off-grade product, and product were dumped into Glynn County estuaries, landfills, dumps, and fugitive emissions from the Hercules Plant into surrounding neighborhoods.

3. EPA Region 4 has structured their entire Response to the OIG Audit around the Simon and Manning article to the exclusion of the many studies about chlorinated camphene and its toxicological effects. EPA Region 4 contends: *"The OIG introduced the Region to the MATT report as the sole information on the toxicity of weathered toxaphene."*
For EPA-Region 4 to represent that the OIG did an exhaustive search of the scientific articles published concerning the toxicological properties of chlorinated camphene is a gross misrepresentation. Even more egregious is for EPA Region 4 to represent that the OIG stated there is only one scientific article concerning weathered toxaphene. Still, EPA Region 4 has claimed that the MATT study is the toxicology model, and used it as their rationale for their Response and the Simon and Manning study.

4. The proposed toxaphene quantification method using only p-26, p-50 and p-62 congeners that is proposed by EPA Region 4 is a re-packaging of the Toxaphene Task Force (TTF) method and will result in a larger under quantification of chlorinated camphene than the TTF method.
The OIG identified the TTF as an inappropriate analytical method since it failed to identify and quantify chlorinated camphene. The OIG found the TTF method was estimated to report as little as 10% of the actual levels of chlorinated camphene present, failed to identify or report Hx-Sed and Hp-Sed chlorinated camphene, and relied only on the latter peaks for quantification, which resulted in a gross underreporting of the actual levels of chlorinated camphene present. The toxicologist with the Agency for Toxic Substance and Disease Registry (ATSDR) noted that use of the "back half" peak method (TTF method) is likely to result in significant underestimation of PCC concentration, and the estimated dose could be 10 times higher if historical data are taken into account for dose estimation.[i] The OIG interview with Dr. Keith Maruya for the Hercules 009 Landfill Superfund Site Five-Year Review resulted in an estimation of toxaphene levels up to 10 times higher than reported by the TTF analytical method. The three congeners proposed for quantification use - p-26, p-50 and p-62 - are located in the latter area, or back-half, of the chromatogram and will exclude Hx-Sep and Hp-Sed chlorinated camphene, which the OIG identified as being important to quantify.

5. Neither the OIG or EPA Region 4 provide toxicological data in support of excluding all chlorinated camphene congeners, other than p-26, p-50 and p-62, from consideration in risk assessments. Sites in Glynn County contain chlorinated camphene manufacturing wastes, off-grade product, and decades of releases into the estuary, landfills, dumps, in

addition to fugitive emissions from the Hercules Plant into nearby neighborhoods. The arguments presented by the OIG and EPA Region 4, that are based upon seafood data, are not relevant when the underlying data is examined and compared to actual conditions present in Brunswick, Glynn County, Georgia. The following comments explore the inconsistencies in the OIG and EPA Region 4 reasoning that led to the conclusion that only p-26, p-50 and p-62 congeners are relevant to the protection of human health and environmental resources in Glynn County.

6. EPA Region 4 stated in their Response, "At this time, the Region considers Simon/Manning as the authoritative article on the toxicity of the degradation products. It focuses on p26, 50, and 62."

Since EPA Region 4 has declared the "...Simon/Manning as the authoritative piece on the toxicity of the degradation products," the article should be closely examined for its adherence to the principals of scientific investigation and reporting. The GEC also asked for other recognized authorities on chlorinated camphene to review and comment on the arguments presented, data and studies used to construct arguments and conclusions, and the quality of the scientific investigation conducted by the authors. The GEC submits the following comments concerning the Simon and Manning article as additional comments to those solicited from experts in their field.

7. The quantification method proposed by EPA Region 4 will report between 1.56% and 8.69% of the chlorinated camphene present, according to the Simon and Manning article.

Failing to quantify between 91% and 99% of the chlorinated camphene present in environmental samples results in a significant and unacceptable degree of uncertainty for any risk assessments produced with the data. Simon and Manning quantified chlorinated camphene congeners p-26, p-50 and p-62 in fish that were exposed by two very different routes, which resulted in very different ratios of congeners, and therefore, very different risk potentials.

8. Dumped Chlorinated Camphene Exposure Route (Simon and Manning, Table 7)

In the seafood samples from the Terry Creek Dredge Spoil Areas/Hercules Outfall Site in Brunswick, Georgia, exposure was from chlorinated camphene manufacturing wastes and chlorinated camphene that was dumped directly to Terry Creek from 1948 to 1970, and additional discharges from residual chlorinated camphene in the Hercules Plant soils, in excess of 8%, continue in 2006. When p-26, p-50 and p-62 congeners were measured in seafood, they ranged from 1.56% to 8.69%, and the average was 4.80%. The p-26, p-50 and p-62 congeners are not the most prevalent in Brunswick, Georgia, and are inappropriate for use as chlorinated camphene indicators.

9. Atmospherically Distilled Chlorinated Camphene Exposure Route (Simon and Manning, Table 6)

Both the OIG and EPA Region 4 relied heavily on the MATT Report[i] for their reasoning and conclusions regarding toxicity. The MATT study investigated levels of chlorinated camphene congeners in seafood exposed by chlorinated camphene that had been atmospherically distilled and transported, which resulted in a very different ratio of chlorinated camphene congeners with very different risk potentials than the ratio of congeners found in Glynn County, Georgia. Individual chlorinated camphene congeners will volatilize and precipitate differently, depending upon the congener's specific chemical properties and atmospheric variables. The result of this atmospheric distillation is selective transport and selective precipitation of individual congeners.

The range of p-26, p-50 and p-62 congeners found in fish exposed via atmospherically distilled chlorinated camphene ranged from 8.02% to 58.05%, and averaged 22.45%.

The MATT study selected the -26, p-50 and p-62 congeners for analysis because it had previously been determined that they were the most prominent in the seafood from the area being studied. The prominent chlorinated camphene congeners in manufacturing wastes in Glynn County are very different, with Hx-Sed and Hp-Sed being the most prominent. Simon and Manning fails to conduct any analysis of what congeners are appropriate for areas contaminated by manufacturing wastes.

10. Dioxin is a component of chlorinated camphene manufacturing wastes and must be taken into consideration when planning sampling, analysis, and risk assessments. Simon and Manning ignores the known additional toxicological properties of chlorinated camphene manufacturing wastes. Chlorinated camphene manufacturing wastes contain their own unique composition of congeners, compounds, and contaminants that must be considered when evaluating risk to human health and the environment. The simplistic approach to chlorinated camphene identification, quantification, and risk assessment presented by Simon and Manning will pose a significant threat to human health and the environment.

11. The use of p-26, p-50 and p-62 congeners is used as an indicator of chlorinated camphene in areas where they are the primary congeners. The primary analytical use of p-26, p-50 and p-62 congeners is as an indicator of chlorinated camphene and not as an quantification or risk assessment tool. [i] The MATT study found relevance in the p-26, p-50 and p-62 congeners only because exposure is exclusively from seafood exposed to atmospheric distilled chlorinated camphene, which results in higher percentages and ratios of the three congeners in northern climates.

12. The range of p-26, p-50 and p-62 congeners vary widely in seafood so total chlorinated camphene is measured for toxicological evaluations. The range of chlorinated camphene congeners can range widely, but as a rule, the higher in the northern latitudes the seafood was obtained, the greater the percentage of p-26, p-50 and p-62 congeners. The use of p-26, p-50 and p-62 congeners is less useful as an indicator for seafood from southern latitudes. [i] Total toxaphene is measured when a risk assessment is being conducted. [i] Tables 6 and 7 in the Simon and Manning paper demonstrate the significant decrease in p-26, p-50 and p-62 congeners in Glynn County, which has been noted in other studies.

13. The comparison of seafood exposed to dumped versus atmospherically distilled chlorinated camphene is inappropriate. Simon and Manning violate the basic principles of scientific investigation by drawing conclusions between dissimilar data sets, and failed to report that the route of exposure of the seafood in the data sets were vastly different. This omission invalidates all conclusions derived. The injection of so many variables, and the failure to report these variables, draws into questions the conclusions reached by Simon and Manning. A review of literature would have revealed that use of p-26, p-50 and p-62 congeners is inappropriate for southern latitudes.

14. Failure of Simon and Manning to report variables such as mode of exposure in the data sets that were compared, and failure to report the ratio of all chlorinated camphene congeners present in seafood Tables 6 and 7 undermines the article to the point that no

conclusions can be reached, nor should the premise presented for risk assessments be utilized. The failure to follow basic scientific investigative techniques and report variables in the data set renders the conclusions and recommendations unusable. If the Simon and Manning method of chlorinated camphene quantification and risk assessment is implemented, it would present significant risks to human health and the environment.

15. As manufactured, chlorinated camphene contains over 800 different chemicals that are found in different ratios depending on the source, latitude, and other environmental factors. Reducing toxaphene quantification and risk assessment to only p-26, p-50 and p-62 congeners ignore these environmental factors and the variables that need to be taken into consideration when conducting human and environmental risks assessments, and remedial decision-making. Environmental sampling should, at a minimum, report all chemical compounds present in the environment. There is no scientifically sound reason for not reporting chemicals present in the environment.

16. Simon and Manning appears to be written as an advocacy of limited testing at the other Sites in County that received chlorinated camphene manufacturing wastes, off-grade product, and other residues of the manufacturing process. These Sites represent significant exposure routes via air, soil, and different congener ratios that are not normally encountered outside of communities where chlorinated camphene was manufactured.
All major exposure pathways and sources need to be identified, but the OIG failed to do so in the Audit, and incorrectly speculates that air and soil exposure are practically negligible when stating:

> *"In general, a major factor needed to evaluate the level of risk to human health is to determine the major exposure pathways to toxaphene's degradation products and to determine all potential sources. The Hercules 009 Landfill site is just one off the potential exposure routes. ...The remaining exposure routes (i.e. air and soil are practically negligible)."*

While local fish consumption is a very significant risk factor, chlorinated camphene levels higher than at the 009 Site are spread throughout the community. The following sources of chlorinated camphene should be considered by the OIG before discounting other significant chronic exposure routes and considering the implication presented in the EPA Region 4 Response:

- Hercules Plant: chlorinated camphene levels in the plant site soils exceed 8% and are a significant air and soil exposure risk, via wind blown dust and erosion.
- Areas surrounding the Hercules Plant: chlorinated camphene was found above 64 ppm on an elementary school playground. Significant source areas are suspected to be present in neighborhoods surrounding the Hercules plant site.
- Terry Creek Site: Between 2 and 3 million pounds of chlorinated camphene manufacturing wastes are estimated to have been released into the estuary, some of which is in dredge spoil areas that are a potential air exposure source.
- Chlorinated camphene was reported to be disposed of in the T Street Dump that is located in the estuary, 4th Street Landfill next to the Glynn Schools Stadium, and Old Sterling Landfill.
- Hercules has taken depositions from workers concerning distribution of toxaphene to employees, purchase by Glynn County Parks and Recreation, and Glynn County Schools for use throughout the community.

17. The GEC agrees that compounds that bioaccumulate need to be identified, but applying chlorinated camphene congeners relevant in Europe and northern latitudes to Glynn County that is located in a southern latitude is inappropriate. The OIG and EPA Region 4 erred by focusing on congeners in fish from northern latitudes that are not relevant to the chemicals of concern at chlorinated camphene contaminated Sites in Glynn County. The OIG took an inappropriate leap of logic when writing:

> *"However, five toxaphene congeners (i.e. p26, p50, p40, p41, and p44) are not readily metabolized and excreted and, thus, can accumulate in the human body. ... To evaluate the level of risk to human health, EPA needs to know the concentration of these five congeners and their metabolite precursors in the environment."*
>
> *"Since these five toxaphene congeners represent the long-term chronic toxaphene exposure problem to humans, the toxicity of these five individual congeners and/or mixture of these five congeners needs to be determined in more detail than is currently available in the scientific literature"*

Even though the conclusion of the OIG might be appropriate in another situation, the basis of the logic and underlying data from a dissimilar area that formed the rationale is not appropriate for chlorinated camphene manufacturing sites and areas that received the wastes.

The GEC agrees that there should be concern about these five congeners and more information would be desirable, but the entire chlorinated camphene manufacturing waste mixture is of concern for long-term chronic exposure in Glynn County. As the OIG noted, the toxicology of chlorinated camphene is not well understood, and even less so for manufacturing wastes . The OIG presents no data in support of ignoring the other 800-plus compounds in the chlorinated camphene mixture manufactured by Hercules, or the manufacturing wastes.

The inherent weakness of considering only persistent congeners found in fish from northern latitudes, as borne out in the discussion of Dr. Olson's study, is that short term exposures can have profound effects on offspring. The exposure duration during the study was not long enough to produce effects attributable to bioaccumulation. Potential endocrine disruption by chlorinated camphene compounds or metabolites must remain under consideration as toxic components, as well as other potential adverse health effects noted in the ATSDR Toxicological Profile for Toxaphene. Synergistic effects of the chlorinated camphene compound in Glynn County could be much different than those noted in studies since both chlorinated camphene and manufacturing wastes are the chemicals of concern. Dioxin produced during chlorinated camphene production could significantly increase the cancer potential of the chemicals present in Glynn County toxic sites.

18. Dr. Gill's and Dr. Barr's studies discussed by the OIG are interesting, but the OIG failed to note that the source was airborne chlorinated camphene transported to Canada in Dr. Gill's study and the general population in Dr. Barr's study, and not exposure to PCC and manufacturing waste products. The same mistake was repeated in the EPA Region 4 Response and by Simon and Manning. Sampling of the local Glynn County population will be needed to confirm any applicability between the results Dr. Gill and Dr. Barr presented and the very different situation that exists in Glynn County. By no means should the need for additional studies or information be used as an excuse not to take action to protect the citizenry of Glynn County from widely distributed chlorinated camphene and manufacturing wastes.

19. The OIG made specific recommendations about which chlorinated camphene congeners should be identified and quantified. The EPA Response limits the selection of congeners to only those in the back-half of the chromatogram window, which is a repackaged version of the Toxaphene Task Force method that will quantify even less of the chlorinated camphene present. Interestingly, and borne out in the OIG audit and the Simon and Manning paper, the p-26, p-50 and p-62 congeners are not prevalent in Glynn County. The OIG's report recommended the following, which includes the prominent congeners, in addition to identification of all chlorinated camphene in the environment.

> *"Since toxaphene is known to degrade in the environment and these degradation products are thought to be toxic, EPA must evaluate the groundwater at the Hercules 009 Landfill site for toxaphene's degradation products, specifically, the Hx-Sed and Hp Sed congeners, but also the p26, p50, p40, p41, and p44 congeners."*

20. The OIG made sweeping conclusions about which compounds in the chlorinated camphene mixture manufactured by Hercules are of toxicological concern based upon data from fish from northern latitudes, and made inappropriate recommendations concerning chlorinated camphene analysis to a few selected compounds. The EPA Response seized upon the congeners and studies identified by the OIG to craft a more limited chlorinated camphene congener quantification and analysis presented in the Simon and Manning paper.
The OIG previously stated:

> *"Conducting a detailed and comprehensive risk assessment for the potential exposure to toxaphene from the Hercules 009 Landfill site is a complex task that is beyond the scope of this OIG review."*

The sweeping recommendations for limited congener analysis do require a comprehensive health assessment and evaluation of literature far greater in scope than presented in the OIG Report or the Simon and Manning paper. At a minimum, ATSDR and natural resource trustees should review any proposed analysis, quantification, and risk assessment procedures for chlorinated camphene. The OIG should clearly recommend that all chlorinated camphene and degradation products will analyzed, identified, and reported in samples from Sites in Glynn County.

21. The OIG identified the need for further research into carcinogenicity and embryotoxicity, but the scope of the research should not be limited to congeners that are not relevant to the chlorinated camphene and manufacturing wastes present in Glynn County. The toxicology of chlorinated camphene is not well enough understood to limit the scope of research at this time, and the toxicology of chlorinated camphene degradation products is even less understood. Regardless of any recommendations for further research, measures should be taken to determine the current human health risks through appropriate testing and the precautionary principle applied until research results are produced, reviewed, and published in a recognized peer reviewed scientific journal that are relevant to the chlorinated camphene congeners and manufacturing wastes present in Glynn County.

22. Glynn County has been identified by the Georgia Department of Human Resources, Division of Public Health, as an area with an incidence of disease above the State of Georgia and National averages, which is noteworthy. Glynn County demographics indicate that the majority of African Americans live in the areas most contaminated by chlorinated camphene and subsistence fish in areas coatmiated by chlorinated camphene. The following health facts should be considered when evaluating chlorinated camphene exposure in Glynn County:

- Childhood leukemia mortality rate in all black males is twice the Georgia average, 14.1769 in Glynn County, compared to 7.6755 in Georgia per 100,000. Childhood leukemia rates are higher in Glynn County for all demographic groups than the Georgia Average.
- Adult lymphoma rates in Glynn County are higher for all demographic groups, except white females.
- All cancers, chronic obstructive pulmonary disease, and liver disease in Glynn County are higher than the national averages. **The liver is a known target organ of chlorinated camphene.**
- Infant mortality and low birth weight rates are higher in Glynn County than national rates.
- The Georgia Department of Human Resources, Division of Public Health has identified Glynn County as having a significantly higher incidence of cancer than the state rate.

23. Children attending schools located next to chlorinated camphene contaminated areas show decreased IQ scores that increase with age. As noted in animal studies, chlorinated camphene has been demonstrated to cause developmental delays. School children attending schools near chlorinated camphene contaminated sites in Glynn County scored lower than children attending other schools. IQ should remain a constant, but as the children grew older the IQ scores rose, which indicates an environmental factor delaying learning potential. Further study is needed of the population that has been chronically exposed for several generations to chlorinated camphene and manufacturing wastes, including impacts to offspring and learning potential.

[1] Health Consultation - Terry Creek Dredge Spoils Areas/Hercules Outfall Brunswick, Glynn County, Georgia. Agency for Toxic Substance and Disease Registry. December 7, 1999.

[2] MATT, 2000. Final Report, Investigation into the Monitoring, Analysis and Toxicity of Toxaphene in Marine Foodstuffs FAIR CT PL.96.3131.

[3] Oetjen, K., H. Karl, Levels of toxaphene indicator compounds in fish meal, fish oil, and fish feed. Chemosphere. July, 1998.

[4] Oetjen, K., H. Karl, Levels of toxaphene indicator compounds in fish meal, fish oil, and fish feed. Chemosphere. July, 1998.

5 Chan, H. M., F. Yeboah. Total toxaphene and specific congeners in fish from the Yukon, Canada. Chemosphere. August 2000.

Attachment D

Review and Comments on the paper "Development of a reference dose for the persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion" by Simon and Manning[i]

This article seeks to redefine environmental toxaphene monitoring by using only tumor promotion as the effect of toxaphene exposure. Further, the authors propose using only three of the several hundred compounds that make up toxaphene as indicators of toxaphene in all media. The paper provides no new experimental observations, no new survey data, and no new calculation algorithms. Instead, the authors use a subset of toxaphene publications to support their views.

The Simon and Manning paper defines toxaphene as all of 800 different chemicals possible for the chlorination of camphene. We concur with this description, as Hercules Incorporated, the manufacturer of toxaphene, stated in their original patent that toxaphene is random chlorination of a nonspecific mixture of camphenes derived from pine stump tar. None of the toxaphene in the environment was ever produced from site specific chlorination of a defined organic carbon skeleton. In just the sixth line of the first paragraph of this paper the authors clearly state that Technical Toxaphene (or "TT") "…consists of a mixture of up to 800 different chemicals…" In the third paragraph the authors offer definitions for Technical Toxaphene (TT) and weathered toxaphene (WT), with weathered defined as degraded Technical Toxaphene. Since there are only about 800 possibilities for toxaphene congeners (the individual chemicals in toxaphene), and the authors have already stated that these make up TT, weathered toxaphene is just a form of technical toxaphene by their own definition. Their descriptions of TT and WT by no means form an inclusive list of the potential forms of toxaphene that may be encountered in the environment. Toxaphene manufacturing waste dumped in streams and borrow pits in Brunswick, Georgia, for example, is toxaphene by the definition in the sixth line of Simon and Manning. Further, the "toxaphene-like" compounds found on schoolyards and in neighborhoods throughout Glynn County, Georgia, also meet the definition of technical toxaphene as defined by Simon and Manning. Essentially, with this definition there is no need for any definition other than "TT" for toxaphene found anywhere on earth; and we concur with their definition.

Simon and Manning Model based on Tumor Promotion

Simon and Manning argue that toxaphene monitoring should be based solely on tumor promotion. The authors provided three arguments in support of their logic: lack of mutagenicity; lack of significant developmental defects; and, carcinogenicity.

Mutagenicity of Toxaphene

The authors' statements regarding toxaphene genotoxicity—the ability to cause genetic damage--in humans are confused and uncompelling. Two points in this regard: it is well-known that microbial studies on mutagenicity, chemically induced damage to DNA, are not directly transferable to humans; and animal exposure studies for lethal doses and minimal effects dose may not produce death or tumors in a manner similar to human physiology. Carcinogenicity, the formation of tumors, is a complex subject, typically, the process requires damage to cellular DNA, but not always, and some chemicals that participate in this process are promoters, not initiators, in the sequence of tumor formation. Since science cannot, at this time, always predict a chemicals' carcinogenicity, best practices require that, if any type of study points to potential genotoxicity, then the material is presumed genotoxic until proven otherwise. The requirement for solid and substantial proof of the absence of a human effect is not found within the arguments of Simon and Manning.

The science proving that toxaphene is genotoxic in bacterial systems is compelling. TT is mutagenic in the Ames test, a widely-accepted bacterial test for quantifying DNA damage. Additionally, there are numerous other bacterial systems where toxaphene is proven to damage DNA. These studies have been reproduced in many laboratories. There is no ambiguity that toxaphene causes DNA damage.

There are two studies regarding chromosomal aberrations in humans cited by Simon and Manning. One was a study of eight field workers accidentally exposed to airborne toxaphene[i] from a spraying incident that found evidence of genotoxicity. A second study[i], examining agricultural workers who may or may not have been exposed from working around toxaphene, did not find evidence of genetic damage.

Visual damage to chromosomes, the organized complex of DNA and proteins within each cell visible during cellular division, is a good indicator of genotoxicity. Simon and Manning correctly note that toxaphene induces sister chromatid exchanges, one form of genetic damage. These studies have been repeated in numerous laboratories and show unequivocally that toxaphene is genetically active in mammalian cells. In reference to the agricultural workers, in both studies potentially exposed workers were monitored by drawing blood samples, separating the white blood cells into culture medium, and examining the rapidly dividing cells. Typically though, any damage or "aberrations" occur from acute injury at high chemical doses and only appear in blood cells for a brief period after exposure. Simon and Manning cite the inconsistency between the two field studies as proof there is ambiguity over toxaphene and chromosome damage. However, field studies of accidentally exposed workers are independent studies, not laboratory controlled studies, and each exists separate from the other. There are no correlations within the studies between toxin dosages; cohorts (age, sex, size, diet, etc.); there are unequal sample sizes; and no control on when and how chromosomes are derived from blood cells. Under these conditions the parameters are all variables; thus, one study cannot be used to refute the other as Simon and Manning have done. The absence of gross chromosomal aberrations in one field study cannot be used to refute the evidence of chromosome damage in other field workers exposed to high levels of toxaphene. Nor does the absence of gross chromosome aberrations in some exposed workers refute, disclaim, or render ambiguous the numerous SCE laboratory studies. Scientists have rules for comparing data sets; Simon and Manning ignored those rules to reach the conclusion they preferred.

Developmental Effects of Toxaphene

Both in *vitro* and *in vivo* (laboratory studies using isolated cells or whole animals respectively) show that toxaphene, and individual congers, cause developmental effects. There is no dispute among scientists that toxaphene changes the way organ systems develop in growing animals. Simon and Manning argue in section 2.1.2 of their paper that doses that induce developmental effects can be used as a not-to-exceed level for toxaphene in the environment. The authors did not provide a predictive model or calculation for this approach. Simon and Manning cite four references, two laboratory studies on toxaphene exposure in rats, and two studies on toxaphene levels in the blood plasma of Inuit women, in support of their dosages. We could not figure out, from the information provided, how they calculated safe dosages for toxaphene from the combination of these four monographs. That 100 ng/ml is useful as a reference for toxaphene in the environment is a highly ambiguous claim by these authors, and it should be ignored without greater support from the literature.

Toxaphene and Cancer

Toxaphene is carcinogenic. In vivo studies show toxaphene causes cancer in laboratory animals. It is interesting and significant that Simon and Manning do not cite studies that show toxaphene is clearly carcinogenic. We restate these findings here:

"Two long-term carcinogenicity bioassays with toxaphene have been performed in rats and mice with both species showing a carcinogenic response."
"A statistically significant dose-related increased incidence of thyroid tumors (adenomas and carcinomas) was seen in both male and female rats."
"A statistically significantly increased incidence of liver cancer in treated animals was observed and was dose-related[i]*."*

The only question is whether or not toxaphene also causes cancer in humans. Simon and Manning offer no models or observations that disprove or prove a link between toxaphene and human cancer.

Existing models for cancer—including the types of carcinoma cited by Simon and Manning--involve a multi-step progression from normal cell to genetically damaged cell, followed by growth proliferation, followed by metastasis. The presumption is that carcinogenic compounds (mutagens and promoters) must be present at genotoxic levels at each stage of neoplasm initiation and promotion. There is also a presumption in cancer models that most cancer onset is a multi-year, and in many cases, multi-decade process. Further, it is a tenet of cancer modeling that there are genetic predilections for certain cancers within human subpopulations, and also genetic resistances to some cancers within racial and ethnic subgroups.

As already noted, toxaphene is mutagenic and, therefore, the potential to cause the mutations that lead to cancer is a possibility. Simon and Manning correctly note that toxaphene is a tumor promoter. Numerous studies using a variety of tools show that toxaphene acts to interrupt normal cellular communication, one definition of a tumor promoter.

After failing to cite data on mutagenesis and tumor production, Simon and Manning calculate an exposure value for tumor promotion based only studies in rats. They could only reach this point in their model by ignoring relevant science that refutes their hypothesis. The authors then further compound this error by citing toxaphene congener levels and the occurrence of breast cancer in Inuit women. The Inuit live in the circumpolar region and have a diet high in fish stocks.

Simon and Manning have incorrectly and unscientifically inferred that levels of toxaphene congeners observed in more recent times have always occurred. In fact, there is no data to indicate what toxaphene levels were in the past in the Inuit subpopulation, TT could have been higher or lower, historically. There is no way of determining present day TT-caused cancer levels based on initiation and promotion events in the past without knowing past exposure levels. For their model to have any relevance Simon and Manning must mistakenly presume the present levels occurred throughout recent history, and, further, there are implied assumptions in their argument that any model for human breast cancer would correlate with rodent models. Also, Simon and Manning have tacitly argued that Inuit are as prone to any TT-induced tumors as the general population. That Inuit women have comparable rates of TT-induced cancers as compared to the general population is practically prophetic on the part of Simon and Manning. Inuits may be more at-risk, or less-at risk, based on dietary, environmental, or genetic factors. That the Inuits experience constitutes a proof of their model is an extraordinary claim that requires extraordinary proof, and Simon and Manning offer no proof.

∑3PC

Simon and Manning chose three of the several hundred toxaphene compounds to base testing for environmental toxaphene: p-26, p-50, and p-62. More data and field surveys are needed to determine if these three compounds are indicative of dietary fish residues. For aquatic food chain and rain deposition (atmospheric reflux) these compounds may indeed prove useful for monitoring food stocks, after more data has been collected and evaluated. However, to make the leap from blood plasma levels caused by eating contaminated fish caught near the Arctic Circle, to soil cleanups in the southeastern US, is scientifically invalid.

We concur that the logic of the approach has merit; there may be a set of TT congeners that are especially indicative of the presence of TT in both TT standards and weathered or off-grade materials that can be used. However, the three selected by Simon and Manning are arbitrary at this junction when applied to soil cleanups; the authors offer no data, nor is there any in the literature. More science is needed before any conclusions can be drawn.

Summary

The Simon and Manning paper raises several issues related to analysis of environmental toxaphene. Unfortunately, the authors generalize, speculate, and infer to such a degree that meaningful conclusions cannot be drawn. One of greatest dangers in research is to assume what one is trying to prove. Assuming at the outset, that a particular conclusion should result, inevitably introduces bias in the conclusions. The preference amongst researchers is for any conclusion to result independently from well-planned and well-controlled experiments. When one proceeds entirely from the basis of literature, from dogma, or experience there can be no such independent conclusion; since one has selected the literature, the dogma and only those experiences that are believed relevant to the desired conclusions.

Such bias is evident in the Simon and Manning paper. The authors state from the outset their intention to prove that just 3 of 800 toxaphene congeners can be used to determine the safety of soil at any cleanup site anywhere in the world. The authors argue that these three congeners are predictive regardless of the origin of the toxaphene, regardless of the form of environmental degradation, regardless of any extraction or instrument bias. In the process of selecting studies to support their view Simon and Manning ignored facts that disagree with their model.

Toxaphene is a highly toxic biocide. Toxicity is an endpoint that must be monitored in any cleanup. Scientifically valid and reproducible studies show wide-ranging mutagenicity in Ames test and cancer in rats. Other studies conclude it is at least likely TT causes chromosome damage in humans. The authors' tunnel vision on three congeners is inappropriate given the unlikelihood all of the toxic and genotoxic effects could be explained by just 3 of 800 congeners acting alone, or in concert. It is more logical to presume, in the absence of hard data, that these multiple effects occur from different isomers in the complex mixture, and that different compounds may affect different animals or plants.

Studies on the Inuit Indians do not exonerate TT as a potential source of carcinogenic chemicals. At this time, the numerous studies showing increases in breast cancer and other tumors in the Inuit have not been traced to a single source. Therefore, a contribution by TT to the overall cancer rate cannot be overruled. Further, this single endpoint cannot be the sole determining factor for soil cleanup in North America. Superfund law is based on multiple criteria: meets all laws; implementability; state acceptance, community acceptance; feasibility; reduction in toxicity, mobility, or volume; and, overall health of humans and the environment. Superfund criteria clearly state that is the overall health of humans and the environment, not just humans, that must be considered. The authors have not shown that cleanup endpoints derived from humans near the artic circle could be protective for other species in North America. Without more hard physical data there is little difference between using the Region 4 Environmental Protection Agency's discredited toxaphene task force (TTF) methodology and the model described in this paper.

Conclusions and Recommendations

At this point in time, it is very clear that lines are drawn between the Region 4 EPA and practically everyone else regarding toxaphene analysis for the purposes of cleaning sites in the southeastern USA. The EPA seems intent on using the toxaphene task force methodology, or its Simon and Manning clone. On the other side are numerous environmentalists and academic scientists, with similar credentials relative to the EPA, who argue current practices underreport toxaphene. Finally, there is the EPA's own Ombudsman who has tried to find the best available science and apply it to this case; however, in the years that the Office of Inspector General has been involved little progress has been made. It appears Region 4 will continue to use some variation of the discredited TTF method unless it can be shown, without equivocation, by some third party, neither EPA nor environmental, that the toxaphene measurement technology Region 4 is using cannot, and will not, work.

We note that the National Research Council of the National Academy of Sciences can undertake the studies needed to clarify toxaphene measurement in the environment. The NRC has undertaken chemical-specific studies on asbestos, dioxin, trichloroethylene (TCE), and on numerous other environmental issues. Progress on cleaning the environment of toxaphene will not be made until toxaphene is defined; debating that definition has become an endless process. A third-party should be consulted and there is none more accepted than the NRC. We recommend that the Glynn Environmental Coalition seek to have a thorough review of toxaphene by a committee of the National Academy of Sciences.

R. Kevin Pegg, Ph.D.

[1] Simon, T. and R. Manning. 2006. Regulatory Toxicology and Pharmacology.
[2] Samosh, 1974.Tsitol Geneti. 8, 24-27.
[3] USEPA, 1978. OPPTS.

[4] From: http://www.epa.gov/IRIS/subst/0346.htm

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Attachment E

Comments on the Reliance of USEPA Region 4 on Simon and Manning, 2005[i] in Decisions Regarding the Hercules 009 Landfill Superfund Site in Brunswick, Georgia

Kathleen Burns, Ph.D.[i]

The U. S. Environmental Protection Agency Region 4 responded in June 20, 2006 to the EPA Office of Inspector General report, "Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia," Report 2005-P-00022, September 26, 2005. EPA relied upon the article, "Development of a reference dose for the persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion," by Simon and Manning, to support their arguments regarding the management of the Hercules 009 Landfill Superfund Site.

The following comments on EPA Region 4's reliance on Simon and Manning, specific issues within the Simon and Manning article, and other issues addressed below were written and are being submitted to the Office of the Inspector General of the US EPA at the request of the Glynn Environmental Coalition (GEC). These comments are pertinent to consideration of some specific health impacts addressed in previous documents by Region 4 EPA, the cleanup of toxaphene from areas where public health or environmental damage may occur due to its presence, and the overall approach taken by US EPA in regions across the country with respect to consistent and reliable application of protective policies.

Topics included in these comments include: the use of epidemiological information in the Simon and Manning paper (and reliance on that information by Region 4 EPA), the apparent lack of adherence by Region 4 EPA to US EPA guidance regarding the exposure of children to mutagenic carcinogens, and the apparent inconsistency that the proposed actions may generate within the Agency with respect to toxaphene. I have also addressed the issue of considering all congeners of toxaphene because it is essential that the full spectrum of hazards and relevant materials be considered when evaluating the risks and establishing protective cleanup levels. This is not addressed in detail here due to the submissions anticipated by other parties and scientists on this issue.

I. The argument presented on using breast cancer rates among Inuits as a basis for establishing a frank effect level.

Relevant data on the increases in breast cancer among Inuits were not presented.

Simon and Manning use an association to address causality, which is never a legitimate use of epidemiological data, and is especially inappropriate for a multifactoral disease such as breast cancer. They note that Inuits are exposed to toxaphene at higher rates than the US population, (up to 4 ug/l in plasma), and conclude:" The Inuit have approximately twentyfold lower breast cancer rates than comparison population so clearly this concentration is less than a frank effect level."

No cancer researcher or epidemiologist would find that statement even plausibly relevant. There are known substantial differences in genetic susceptibility to breast cancer (and other cancers) and many of the risk factors for breast cancer that are present in the mainland US are not present in the Inuit occupied areas, including many air and water pollutants. The National Library of Medicine lists over 450 scientific journal articles on various breast cancer risk factors published within just the last five years (search conducted August, 2006).

I have summarized some relevant evidence demonstrating that the Simon-Manning claim is irrelevant, primarily addressing the fact that there have been increases in the rates of breast cancer among Inuit women subsequent to the introduction of toxaphene into their environment (though no causal argument is made here).

The increasing incidence of breast cancer in the second half of the 20th century among Inuits is of serious concern. "The incidence increased from 28.2 per 100 000 in 1969-1973 to 34.3 per 100 000 in 1984-1988." (Miller and Gaudette, 1996). Over a 15 year period, that is an increase in 22% in the rate of breast cancer among Inuits.

A subsequent study considered the breast cancer rates among Inuits moving forward into the late 1990s, comparing two periods: 1973-1987 and 1988-1997. Using gender specific age adjusted cancer rates, the researchers found: "The incidence of lung, stomach, breast and colon cancer increased" (Friborg et al, 2003).

Thus, there is clearly an increase in breast cancer rates among Inuit women and also increases in other potentially lethal cancers among the Inuit people. The importance of this is underscored when the relative isolation and past health of these people is considered. This is best illustrated by the following very disturbing statement made over 20 years ago on the situation with respect to Canadian Inuit women:

> Breast cancer was absent before 1966 and was found in only 2 of 107 Canadian Inuit women stricken with cancer from 1967 to 1980, whereas the recent rates in the longer-acculturated Inuit of Alaska and Greenland have approached those prevailing in modern Western women.

(Hildes and Schafer, 1984)

A spectrum of cancers are of concern with respect to toxaphene, not merely breast cancer.

The occurrence of breast cancer is not the primary focus of concern for human cancers as the following indicates:

"As mentioned previously, toxaphene is carcinogenic in rats and mice and also has been proven to be mutagenic (*1,178*). Such findings have led to the assumption that toxaphene poses a risk as a human carcinogen. Human exposure to toxaphene occurs mainly through the consumption of contaminated fish or by occupational exposure. Data are scarce on the risk to humans from toxaphene exposure (*1*). Brown et al. (*228*) and Cantor et al. (*229*) evaluated the association between elevated risk of leukemia and non-Hodgkin's lymphoma (NHL) among farmers and exposure to pesticides and other agricultural chemicals and concluded that there is an elevated risk of NHL among farmers. Risk increased in cases in which farmers personally handled, mixed, or applied pesticides, did not use protective clothing, and when more specific active mixtures of pesticide exposure were used. Chemicals most strongly associated with risk of NHL were carbaryl, chlordane, DDT, diazinon, dichlorvos, lindane, malathion, nicotine, and *toxaphene.* " (de Geuss et al, 1999)

Evaluations of lymphomas and leukemias have not been extensively carried out among the Inuits, but there is some evidence available. Historically, Inuit peoples in have had a low risk for lymphatic and hematopoietic malignancies, including non-Hodgkin lymphoma, Hodgkin's disease, multiple myeloma and the combined leukaemias. However, Inuits women have had an increase in hematopoietic system cancer (leukemias) during the second half of this century (Lanier and Alberts, 1996). It is noted by this author that women typically have a higher body fat composition, and toxaphene congeners are lipophilic substances that seek, deposit in, and bioaccumulate in body fat. While no single cause can be identified as the reason for increase leukemia rates among women in this population, it is noted that the increase occurred during a period when levels of many persistent organic pollutants were increasing in the global environment.

Overall, the well documented and very troubling increases in cancer among Inuit and other polar communities prompt serious concerns about causality. It is notable that these increases correlate in time with increased Persistent Organic Pollutants (POPs) present in their food supply during the post-WWII period, including toxaphene. And although no causality can be implied from time correlations, they do raise public health concerns. The lower incidence of breast cancer among Inuits than among other women in the US in no way exonerates toxaphene as a causal agent in breast cancer in the US or among the Inuit population.

II. Requirement for applying an additional factor to consider early life exposures to mutagenic carcinogens

EPA now requires that risk assessments and the establishment of new standards, exposure limits, etc, take into account the increased susceptibility to cancer that is conferred when exposures occur early in life to mutagenic carcinogens. This is fully described with many relevant documents at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283

The EPA requires the use of factors that are expected to range from 3 to 10 and that reduce the amount of a toxic chemical that may be present in order to protect children during the pre and postnatal period. The use of a factor to address this area of health risk is relevant for toxaphene based on information provided below and in other sources.

Toxaphene it is not mutagenic in all test systems; however, it is mutagenic in many. There have been numerous genotoxicity studies conducted over decades by various groups, with tests sponsored by different groups, and it is therefore not surprising that the results are not consistent. De Geuss et al (1999) states, "Toxaphene is carcinogenic in rats and mice and also has been proven to be mutagenic." (excerpt from quote above).

Numerous summaries of the genotoxicity of toxaphene have been provided in journal articles, and in the ATSDR Toxicological Profile for Toxaphene. The following, from de Geuss et al (1999) is brief and relevant:

> "More recently, Steinberg et al. (*224*) tested toxaphene and four toxaphene congeners, B[12012]-(202), B[12012]-(212), B[30030]-(122), and B[30012]-(111),

> for mutagenic activity in *Salmonella typhimurium* strains TA98 and TA100 using a validated microsuspension procedure instead of the usual plate-incorporated procedure. Toxaphene was mutagenic only in the TA100 strain at concentrations of 2,500, 5,000, and 10,000 μg ml^{-1}. In contrast, toxaphene was also mutagenic to strain TA98 at a concentration of 10,000 μg $plate^{-1}$ when using the plate-incorporated assay. Using the microsuspension method, none of the four tested toxaphene congeners showed mutagenic activity in strain TA100 at any of the concentrations tested (maximum concentration: 10,000 μg ml^{-1}). A dose-dependent (10-10,000 kg $plate^{-1}$) increase in His revertants was also observed in strains TA97, TA98, TA100, TA102, and TA104 by Schrader et al. (*225*) in the absence of S9 metabolic activation. Genotoxicity of the technical toxaphene, as well as B[30012]-(111), but not B[12012]-(202), B[12012]-(212), and B[30030]-(122), was also demonstrated by Boon et al. (*128*) using the Mutatox assay. Addition of rat S9 fraction or microsomes of harbor seal and albatross decreased the genotoxic potential of the tested congeners and toxaphene. More *in vitro* evidence for genotoxicity was found by Sobti et al. (*226*) showing toxaphene-induced sister-chromatid exchange (SCE) in cultured lymphoblasts. In contrast, Schrader et al. (*225*) could not demonstrate convincing evidence of a toxaphene-induced (1-10 μg ml^{-1}) dose-dependent SCE induction at the HGPRT gene locus in V79 cells.
>
> Knowing that cell-cycle delay may interfere with the expression of genotoxicity, Steinel et al. (*220*) studied the effect of cell-cycle delay on the induction of SCE by toxaphene in Chinese hamster lung (Don) cells. They found that toxaphene exhibited a dose- and time-dependent decrease in cell-cycle progression. At similar concentrations of toxaphene, higher numbers of SCEs were observed and dose and treatment time relationships were demonstrated. Hence, SCE induced by toxaphene was not masked by mitotic delay and longer toxaphene treatment times were not necessary in Don Chinese hamster cells. Nevertheless, the authors support recommendations for prolonged incubation times in SCE assays affected by mitotic delay."

The assertion of genotoxicity is supported by the observation that studies show toxaphene is capable of causing multiple types of cancers in experimental systems (de Geuss et al, 1999). This finding indicates that it is possible that toxaphene induces cancer by more than one mode of action. While there may be some carcinogenic modes of action that do not involve mutations (e.g., promotion via other mechanisms), the evidence supports the use of the EPA-required default assumption regarding cancer induction (USEPA, 2005a, see USEPA Guidelines for Cancer Risk Assessment as summarized in Federal Register: April 7, 2005 (Volume 70, Number 66) Page 17765-17817 at: http://www.epa.gov/fedrgstr/EPA-TOX/2005/April/Day-07/t6642.htm). For mode of action discussions and related Agency risk assessment requirements see especially pages 17788 - 17817).

Industry has not disproven genotoxic mechanisms of cancer induction by toxaphene and EPA policy requires assumption of a mutagenic mode of action for carcinogens in the absence of evidence to the contrary. In fact, given the evidence of mutagenicity, it is unlikely that one could ever prove that toxaphene is incapable of inducing cancer via genotoxic mechanisms. Because the scientific evidence shows that toxaphene has genotoxic potential and is an established carcinogen, the EPA Risk Assessment Guidelines require that it the increased susceptibility that results from early life exposures to this chemical be considered. This is specified in "Guidelines for Carcinogen Risk Assessment and Supplemental Guidance for Assessing Susceptibility from

Early-Life Exposure to Carcinogens" (available at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283 (USEPA, 2005b)

Additional information on this topic and the scientific concepts that support it have been discussed by Barton, Cogliano, Flowers, Valcovic, Setzer, Woodruff (2005), who have all contributed substantially to this EPA policy.

III. Consistency within the agency in the interpretation and use of scientific information in efforts to protect public health.

The information on cancer risk, and resulting guidelines on fish consumption for toxaphene based on its carcinogenic potential are relevant and are substantially different than those shown in the Simon-Manning paper. Internal inconsistencies in the evaluation of science and in the application of protective standards and policies are unacceptable within a federal agency. It is particularly important in areas where environmental justice issues have been raised that full attention be paid to using the protective and precautionary approaches specified in EPA's national policies, as posted in Federal Register notices. The decisions by EPA Region 4 must adhere to Agency policy and scientific consensus.

EPA guidance document on fish contamination concentrations and associated limits on intake when toxaphene is present as a contaminant in fish are provided in "Guidance for Assessing Chemical Contaminant Data for Use In Fish Advisories. Volume 2: Risk Assessment and Fish Consumption Limits - Third Edition at http://www.epa.gov/ost/fishadvice/volume2/v2ch4.pdf (USEPA, 2000). This document resulted from extensive internal and external peer review and represented the position of numerous scientists within the Agency. Volume 3, which addresses risk management for fish advisory programs, also prescribes some degree of precaution and preventative action and encourages local evaluation of exposures (see www.epa.gov for Volume 3).

IV. Consideration of all relevant components and breakdown products of toxaphene

Toxaphene is a complex mixture of chemicals with similar structures, as is the case for most organochlorine pesticides. There are standard approaches that have taken for these pesticides and for other mixtures of similarly structured chemicals (isomers, congeners, etc). These typically rely upon an evaluation of the relative toxicity of each of the components with respect to the full spectrum of potential health hazards (cancer, birth defects, neurotoxicity, immunotoxicity, nephrotoxicity, hepatoxicity, etc), or rely upon studies for each of these types of toxicity that evaluate the full mixture of similarly structured chemicals that comprises the named product.

In addition, US EPA typically requires that a risk assessment of a contaminated site include an evaluation of all of the breakdown products that will be produced under a variety of environmental conditions, and that the toxicity of these breakdown products be fully explored. Thus, the objective is to fully characterize the potential harm that may result from all plausible chemicals formed from the original group of contaminants, as well as from the original contaminant group itself.

US EPA also specifies that mixtures containing chemicals with similar structures and mechanisms of action be considered together in evaluating risk and in determining adequately protective actions. In the case of toxaphene within Glynn County, this should include all manufacturing waste that falls within US EPA specified parameters for similar chemical structures and mechanisms of action. If this is not addressed in decisions made regarding cleanup for Glynn County, the potential risks may be unacceptably high.

There are extensive listed requirements, discussions of the rationale for the requirements, and examples of how all of the above listed issues have been addressed by the US EPA in the past within US EPA's website (www.epa.gov).

With respect to toxaphene, it is imperative that the full spectrum of chlorinated camphenes and the degradation products that occurred as a result of toxaphene be considered in any treatment of toxaphene (e.g., in cleanup levels, establishment of seafood advisories, evaluation of human body burden). The evaluation of the nature and amount of toxaphene present must be done in a scientifically defensible manner that addresses the actual conditions in Glynn County. This should include chemicals present as a result of local environmental circumstances (chemicals that result from disposal on land, releases into air and subsequent deposition, uptake and alterations within biota, interactions soils, air, or water that has specific properties - acidic, basic, etc).

There are straightforward and well established methods for evaluation of toxaphene's spectrum of chemical ingredients and breakdown products specified within US EPA's website and available through a variety of scientific papers. As one of the older pesticides used in the United States, methods that capture the spectrum of congeners comprising toxaphene are well known.

Considering US EPA's past actions on toxaphene and similar chemicals with respect to the protective stance taken, evaluation of the potential hazards, and the need to equitably manage the cleanup of contaminated sites, I urge the Office of the Inspector General to act on behalf of the public in affording the residents of Glynn County the full health and environmental protections to which they are entitled. While not underestimating the challenges this poses to all who are involved in this work, it is in the interests of the people of the County and future generations who will live there that the United States government insure that people will be able to live in a safe and healthy environment.

Respectfully submitted on September 7th, 2006 to Paul McKechnie, US EPA Office of Inspector General, Boston, Massachusetts by Kathleen Burns, Ph.D. of Lexington, Massachusetts via Glynn Environmental Coalition, Brunswick, Georgia.

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USEPA, 2005b. Guidelines for Carcinogen Risk Assessment and Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens .

Attachment F

Comments to OIG on Hercules 009 Superfund Reports October, 2006

October 10, 2006
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Public Interest Comments on the Office of Inspector General Reports: Appropriate Testing and Timely Reporting are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia[1]

Report 2005-P-00022; September 26, 2005
Report 2005-P-00022 (Addendum); September 13, 2005
and

More Information is Needed on Toxaphene Degradation Products[2]

Report No. 2006-P-00007, December 16, 2005

We, the supporters of this letter, advocate on behalf of our millions of members for regulations that provide protection to communities, workers, and wildlife. We do not have any financial interest in the subject of this letter.

Jennifer Sass, Ph.D., Natural Resources Defense Council (NRDC)[1]
Kathy Burns, Ph.D., ScienceCorps
Denny Larson, Director, Global Community Monitor
Kristin Schafer, Pesticide Action Network North America
Michelle Roberts, Beyond Pesticides
Joseph DiGangi, Ph.D., Environmental Health Fund
Ted Schettler MD, MPH Science and Environmental Health Network
Pam Miller, Alaska Community Action on Toxics
Rick Hind, Greenpeace, USA
Nathalie Walker & Monique Harden, Advocates for Environmental Human Rights
Lin Kaatz Chary, PhD, MPH, Indiana Toxics Action Project
Gregg Small, Washington Toxics
Mark A. Mitchell M.D., MPH, Connecticut Coalition for Environmental Justice
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Amanda Hawes, Toxics Chair, WORKSAFE
Stephen Lester, MS, Center for Health, Environment, and Justice
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Mary Brune, MOMS – Making Our Milk Safe

Jeanne Rizzo, Breast Cancer Fund

Summary

The Office of the Inspector General, at the request the Glynn Environmental Coalition, has reviewed claims that a Glynn County, GA Superfund site contaminated with Toxaphene is receiving inadequate clean up. At the heart of the dispute is a testing method that fails to detect most of the toxic congeners and degradation products of toxaphene, thus underestimating the extent of contamination. Use of the biased testing method was approved by a closed partnership between EPA Region 4, the Georgia Environmental Protection Division (GaEPD) and Hercules, Inc. that failed to include community representatives. Both the OIG and a previous review by the Agency for Toxic Substances and Disease Registry (2002), have recommended that EPA should discard this flawed method in favor of established tests that identify toxaphene degradation products.

We generally support the OIG reports, and encourage the OIG to issue a strong response to EPA to work with the community, apply appropriate scientific methods, and force the stringent clean up that was promised to the community over two decades ago when this site, predominately populated by low-income African-American families, was listed as a National Priority Superfund site.

History of the site[3]: *twenty years is too long*

Hercules Inc., a former pesticide plant, manufactured toxaphene as an insecticide at its plant in the city of Brunswick, Glynn County, Georgia, from 1948 to 1980. In these comments, we will use the term "polychlorinated camphene" (PCC) to describe toxaphene, a mixture of over 670 chemicals of concern, and its residues and conversion products.

The Hercules 009 Landfill Superfund Site in the city of Brunswick, in Glynn County, Georgia operated from 1975 until 1980, and was listed on the National Priorities List (NPL) in 1984, over 20 years ago[4]. The Brunswick area has a commercial fishing port and a thriving seafood industry, as well as recreational fishing and crabbing.[9]

The Hercules 009 Landfill is described as a 16.5 acre property that is bordered by Georgia State Highway 25 on the west; an automobile dealership on the north; a juvenile slash pine forest on the east; and several homes, a church, a school, and a strip shopping center to the south/southeast of the property.[5]

Until required by the Clean Water Act to treat waste water in 1972, Hercules reportedly released up to 200-300 pounds of PCC per day as waste water,[6] ranged from 2,332 parts per billion (ppb) in 1970 to 6.4 ppb in 1974.[7] PCC has been reported at levels exceeding 15,000 parts per million (ppm) at the Hercules 009 Landfill Site.[8] In 1976 PCC discharge was restricted to a daily maximum of 1 pound per day and a daily average of 0.5 pounds per day. Subsequent discharge was limited to 0.00081 ppm, though violations were recorded.[9]

In July 1988, Hercules and EPA entered into an Administrative Order on Consent for conducting a remedial investigation/feasibility study (RI/FS)[10] to assess the risk to human and environmental health and evaluate treatment approaches.[11]

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[1] To whom correspondence should be sent. Full contact information at end of these comments.

In 2002, the Agency for Toxic Substances and Disease Registry (ATSDR), an agency of the U.S. Department of Health and Human Services, conducted a public health assessment of some of the Hercules waste areas in Brunswick.[12] In that report, ATSDR recommended limiting consumption of fish from the contaminated areas.

Both the ATSDR and the Office of the Inspector General (OIG) specifically identified the method advocated by EPA Region 4 and Hercules as insensitive, inadequate, and likely to significantly underestimate contamination levels, and instead recommended the use of pre-validated and scientifically accepted measurement methods.[13] [14]

Current clean up issues: ***intentionally insensitive methods fail to detect contamination***
The Hercules Landfill Superfund Site and five other sites contaminated by PCC in Glynn County, Georgia are slated for a sub-standard clean up that will leave at risk the community and the environment. This is being pushed through because of a closed partnership between EPA Region 4 and Hercules that excluded community participation. This pairing of between state regulators and the regulated industry was self-titled the Toxaphene Task Force. Among numerous biased and discredited pronouncements of this task force was use of a measurement method that failed to detect most of the over 600 congeners, residues, and degradation products of PCC contamination. The Region 4 assessment, relying on the flawed method, was strongly criticized by the ATSDR in a 2002 report as underestimating the exposure.[15] The OIG specifically noted that the methods used by Region 4 and Hercules are not designed to measure toxaphene degradation products, and instead recommended established testing methods that specifically test for toxaphene degradates.[16]

The stubborn insistence by Region 4 to continue to rely on a biased and unscientific method that has been rejected by the ATSDR and the OIG can cynically be viewed as a blind, ideological adherence to fiction in the face of facts. The result of these actions, whether ignorant or intentional, is a failure to provide the protection for human and environmental health that is promised in the mission[17] of the EPA.

Hazard information: ***Toxaphene is persistent, bioaccumulative, and banned***

Toxaphene is a toxic chlorinated-hydrocarbon persistent bioaccumulative banned pesticide. It is a mixture of over 670 chemicals of concern, and is approximately 40 to 75% chlorine by weight. In 1982 toxaphene was restricted in the US, and then fully banned in 1990. Although it has low solubility in water, it is readily adsorbed in soil and sediments, and bioconcentrates in aquatic organisms including fish. It is highly acutely toxic to fish, even at concentrations that are low parts per billion (ppb) or high parts per trillion (ppt).[18] [19] [20]

In its 2002 report of the Brunswick area, ATSDR described the relevant toxicity literature. Animal testing showed that pre-birth and post-natal exposure to toxaphene may interfere with normal development.[21] When pregnant rats were fed a diet contaminated with toxaphene, effects included poor righting ability and poor swimming ability, compared with healthy control animals.[22] The exposed rats eventually attained normal swimming ability. ATSDR also noted that, "when the rats took a maze test at the age of 70 days, those previously exposed to PCC components had difficulty remembering the path leading to the food". ATSDR recommended that, "pregnant women and nursing mothers should avoid consuming large quantities of contaminated fish and, obviously, avoid ingesting contaminated soil" to protect the developing fetus and child. ATSDR warned that exposure to PCC through contaminated fish and surface soils, should also be minimized in infants and young children.[23] Air exposures should also be considered hazardous; PCC is up to 8% in soils at the Hercules Plant.

National interest: ***a bad job here may lead to failed clean-ups nationally***

NPL sites are the most serious sites across the country, slated for possible long-term

cleanup by EPA's Superfund program. Altogether, there are 1,246 final sites across the country, of which 18 sites across 9 states include toxaphene as a contaminant.[24] Therefore, the level of clean up that EPA will require at this site is likely to impact requirements across the country.

The document record is clear that it is the intention of Hercules to submit its toxaphene review to the EPA database, the Integrated Risk Information System (IRIS), which contains EPA's scientific positions on potential human health effects from environmental contaminants. While not an enforceable regulatory standard *per se*, information on IRIS is considered by regulators at the state and federal level and others worldwide to set pollution cleanup standards and various exposure standards for air, water, and soil.

Hercules advocated a reduction in the cancer potency factor 10-fold on the IRIS database[25] from 1.1 per mg/kg/day to 0.11 per mg/kg/day, and stated that it has already gone so far as to submit its proposed factor to Office of Solid Waste and Emergency Response (USEPA/OSWER), based on "new information"[26] citing a 1998 report. This would likely severely impair clean-up action at contaminated sites all over the country.

In addition to weakening the cancer potency factor, Hercules also proposed to weaken the non-cancer "safe" level, known as a Reference Dose (RfD), posted on the IRIS database. In its comments to ATSDR, Hercules states that it has submitted an alternative RfD of 0.0007 mg/kg/day for the IRIS database.[27] This is approximately 3-fold more permissive than the old IRIS RfD of 0.00025 mg/kg/day (IRIS, 1993), which has now been removed from the IRIS database. Hercules specifically notes that use of its alternate RfD value would raise the screening level from 3 ppm to 7.5 ppm toxaphene in fish.[28]

It should be extremely concerning to taxpayers that a scientific article that proposes to disregard all but a handful of PCC congeners is co-authored by scientists from EPA Region 4 and the Georgia Environmental Protection Division (Simon and Manning, 2006). Though no source of funding is disclosed, it is published in a journal, *Regulatory Toxicology and Pharmacology*, well-known to be biased towards industry perspectives. In fact, in 2002 the journal was targeted in a letter by over forty scientists, including noted international experts and journal editors, citing concerns about, "apparent conflicts of interest, lack of transparency, and the absence of editorial independence".[29] Specifically, their letter cites, "the journal's apparent bias in favor of industries that are subject to governmental health and environmental regulations". The letter goes on to identify financial supporters of the journal sponsor, including, the American Chemistry Council, Dow AgroSciences, R.J. Reynolds Tobacco Co., and others. Moreover, the letter identified a "significant percentage" of the editorial board with financial ties to companies whose products are the subjects of studies published in the journal. Is it any wonder, then, that this article advocating a weakening of cancer potency of toxaphene found its way to this journal? But, the

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fact that the authors are public employees suggests a concerning level of partnership between Hercules and the regulatory agencies.

Environmental Justice: ***EPA fails to act on Executive Order 12898***

The State and Federal agencies charged with the protection of human and environmental health are faced with a moral test of deciding whether to unfairly burden Glynn County families with health risks that they are not likely to bear themselves, and that are not shared equally across the nation.

Glynn County is comprised of 72% white population and 26.5% black population, more diverse than the National average of 80% white and 13% black (2004 Census data).[30] However, the Brunswick city has a total population of approximately 15,600 people, of which 36% are white and 60% are black (2000 Census data as reported by ATSDR).[31]

(data are rounded off)	Brunswick city (2000 data)[i]	Glynn County (2003/4 data)[i]	US (2003/4 data)[i]
White persons	36%	72%	80%
Black persons	60%	27%	13%
Median household income	$22,000 ($18,400 for black; $27,900 for white[i])	$38,000	$43,000
Persons living in poverty	30%	15%	12.5%

The county has approximately 27,000 households (2000 data), with a median household income of $38,600, less than the National median of $43,300 (2003 data). However, Brunswick City has a median household income of only $22,200 (2000 data), much lower than the county and national. This leaves 15% of Glynn County residents living below poverty (2003 data), more than the National average of 12.5%. However, 30% of Brunswick City residents live below poverty (2000 census data). In summary, Glynn County residents are more likely to be black and/or to be poor than the average American.

In addition to the Hercules 009 Superfund site, the Brunswick area is the site of two additional industrial facilities that have been classified as Superfund sites, and 17 other potentially hazardous waste sites.[36] Maybe the unfair distribution of toxic dump sites and other industrial facilities is a significant factor in the higher rate of cancer and other diseases among black residents compared with white residents of Glynn County. In the health service area that extends from Duval County (Jacksonville) FL to Glynn County GA, EPA reports that the overall cancer rate per 100,000 population is 177 for white males compared with 257.7 for black males.[37] The cancer rate for white females is 118.4, compared with 135.1 for black females. Childhood leukemia rates are almost 2-fold higher for black males (14.1 per 100,000), compared with white males (8.9 per 100,000);[38] data for females is similar for white (6.1) and black (4.9) populations.

The EPA provides a description of environmental justice on its website:

> Environmental Justice is the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. EPA has this goal for all communities and persons

> across this Nation. It will be achieved when everyone enjoys the same degree of protection from environmental and health hazards and equal access to the decision-making process to have a healthy environment in which to live, learn, and work.[39] Despite this laudable and critical recognition of the unfair distribution of risk and disease across this country, a study just released in September 2006 by the Office of the Inspector General is highly critical of EPA's failed record on taking action to correct these injustices.[40] The IG recommended that EPA review its programs appropriately and take action consisted with Executive Order 12898 to address the unfair impact of industrial waste on communities.[41]

Take action now to protect human health

We generally support the OIG reports, and encourage the OIG to issue a strong response to EPA to work with the community, apply appropriate scientific methods, and force the stringent clean up that was promised to the community over two decades ago when this site, predominately populated by low-income African-American families, was listed as a National Priority Superfund site.

Thank you for your consideration of these comments.
Respectfully,

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[1] summary at http://www.epa.gov/oig/reports/2005/20050926-2005-P-00022-Gcopy.pdf full report at http://www.epa.gov/oig/reports/2005/20050926-2005-P-00022.pdf addendum at http://www.epa.gov/oig/reports/2005/20050926-2005-P-00022A.pdf

[2] summary at http://www.epa.gov/oig/reports/2006/20051216-2006-P-00007-Gcopy.pdf full report at http://www.epa.gov/oig/reports/2006/20051216-2006-P-00007.pdf

[3] EPA. Georgia NPL/NPL Caliber Cleanup Site Summaries. http://www.epa.gov/region4/waste/npl/nplga/herculga.htm

[4] CERCLIS ID GAD980556906

[5] EPA. Georgia NPL/NPL Caliber Cleanup Site Summaries. http://www.epa.gov/region4/waste/npl/nplga/herculga.htm

[6] ATSDR. Public health assessment: Terry Creek dredge spoil areas/ Hercules outfall site, Brunswick, Glynn County, Georgia. 2002. http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_toc.html

[7] http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p1.html#backa

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[8] EPA. Georgia NPL/NPL Caliber Cleanup Site Summaries. http://www.epa.gov/region4/waste/npl/nplga/herculga.htm

[9] http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p1.html#backa

[10] Definition of RI/FS http://www.epa.gov/superfund/whatissf/sfproces/rifs.htm

[11] EPA. Georgia NPL/NPL Caliber Cleanup Site Summaries. http://www.epa.gov/region4/waste/npl/nplga/herculga.htm

[12] http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p1.html#backa

[13] summary at http://www.epa.gov/oig/reports/2006/20051216-2006-P-00007-Gcopy.pdf full report at http://www.epa.gov/oig/reports/2006/20051216-2006-P-00007.pdf

[14] ATSDR report (2002) Appendix F: Response to comments. ATSDR states, "On April 14, 2000, ATSDR formally received an analytical protocol from USEPA, Region IV describing the "Procedures for the Determination of Toxaphene," a three-page protocol dated August 14, 1997. This protocol, which was intended to be used by USEPA-Region IV and Hercules, employed "the last four to seven peaks in the 'back half' of the toxaphene chromatogram for calibration and quantification of toxaphene." The "four peak in the back half" methods dates to the packed column days, when there were only several usable peaks shown on the back half of toxaphene chromatogram (USEPA 1986 Method 8080). This "four-peaks-in-back- half" method was precise at that time... This method, however, has lost its precision now because the powerful capillary column in modern gas chromatography instruments generates dozens of peaks in the back half of the chromatogram of toxaphene standard... Although the Method 8081A of January 1995 kept this "four-peaks-in-back- half" method, the method was purged from the official December 1996 version of Method 8081 A, as well as the new Method 8081 B of January 1998. Recently, GA EPD repeated the analysis of 56 samples from the old April 1997 samples with the specific methodology of both GC-ECD and GC-MS at Skidaway Institute of Oceanography. On June 19, 2000, quantitative data for the 56 samples became available and the PCC concentrations up to 26 ppm was found in fin fish. This work was published in peer reviewed, open literature in September 2001." http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p3.html#appf

[15] http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_toc.html

[16] summary at http://www.epa.gov/oig/reports/2006/20051216-2006-P-00007-Gcopy.pdf full report at http://www.epa.gov/oig/reports/2006/20051216-2006-P-00007.pdf

[17] "The mission of the Environmental Protection Agency is to protect human health and the environment." http://www.epa.gov/epahome/aboutepa.htm#mission

[18] Maruya KA and Lee RF. Arochlor 1268 and toxaphene in fish from a southern U.S. estuary. Environ Sci Technol 1998;32:1069-75.

[19] ATSDR report. 2002. http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p1.html#sum

[20] The ATSDR report Appendix F reported that, "The acute LC50 values for other kinds of fish ranged from 2 ppb for basses to 18 ppb for bluegills. PCC in chronic exposure systems were one to three orders of magnitude more toxic to fish than were acute exposure systems. The chronically toxic effects of PCC were observed at 39 ppt in brook trout, and at 36.7 ppt in fathead minnow." http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p3.html#appf

[21] Agency for Toxic Substances and Disease Registry. Toxicological profile for toxaphene. Atlanta: US Department of Health and Human Services; August 1996.

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[22] Olson KL, Matsumura F and Boush GM. Behavioral effects on juvenile rats from perinatal exposure to low levels of toxaphene, and its toxic components, toxicant A, and toxicant B. Arch Environ Contam Toxicol 1980; 9:247-57.

[23] http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p1.html#backa

[24] Query for toxaphene, September 26, 2006. http://oaspub.epa.gov/oerrpage/basicqry

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[26] ATSDR report, 2002. Appendix G. p. 113 http://www.atsdr.cdc.gov/hac/PHA/terrycreek/tcd_p4.html#appg

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Attachment G

EPA OIG Close Out Letter - October 31, 2006

Attachment H

009 Superfund Site - EPA OIG Close Out Letter

By Dr. R. Kevin Pegg

We received for review the response for the EPA's Office of Inspector General to EPA's Region 4 Administrator regarding the analysis of toxaphene at the 009 site. Previously the OIG had found that Region 4 was using methods that underestimated toxaphene in soils, groundwater and animal tissues. As part of that finding Region 4 was to utilize methods in keeping with the state-of-the-art in toxaphene testing, rather than decades-old methods that had been used. Region 4 provided a response to the OIG that raised a number of issues. Principally, Region 4 relied heavily on a position paper prepared by former Region 4 employees, Simon and Manning, on weathered toxaphene (we reviewed the S&M paper in a prior newsletter).

The OIG's response is complex and contradictory. The OIG continues to argue that more research is needed for the toxicology of toxaphene. The report states clearly that much more work on analysis is needed, and urges Region 4 to work directly with the EPA's Office of Research and Development to analyze toxaphene. And, the response urges transparency in the manner in which Region 4 calculates the remediation goals for the 009 site. Then again, the response states that they are dropping the matter as "...you [Region 4 EPA] have adequately addressed the recommendations we made."

The accompanying review by Michael Wilson, a former scientist with EPA that worked for the OIG, is not very detailed. It relies almost entirely on the documents provided by Region 4, and, according to the cover letter, was provided pro bono since the author is no longer at EPA. Regarding the Simon and Manning paper the author indicates it is the best science available because it is the only science available. Further, Wilson could also not calculate a reference dose using the Simon and Manning paper. Nonetheless, the author concludes that Region 4's burden-of-proof is met, despite the fact that he, like everyone else in the scientific community, is clueless as to the meaning and origin of the numbers cited by Region 4 in the S&M paper.

Essentially, one EPA employee has validated other EPA employees' unscientific and irreproducible work. The letters infer no additional effort will made on understanding toxaphene migration in Brunswick until after 2008. Note also, this marks the final report on the 009 Superfund site under the Technical Assistance Grant.

Attachment I

From: Glynn Environmental Coalition

To: Glynn County Board of Education

The Glynn Environmental Coalition (GEC) is providing the following information for your use when discussing the issues surrounding the testing of Altama Elementary School with the Board of Education (BOE). With your background in the environmental sciences, you should grasp the content and implications of the information provided. The EPA Region 4 presentation to the BOE on January 29, 2007, is a continuation of a decision made in 1991 to NOT report all chemicals present by development of an analytical method for toxaphene that is only used in Glynn County, which was found inappropriate by the EPA Office of Inspector General (OIG). The GEC trusts the following information will provide a firm basis for our concerns, which resulted in the EPA OIG agreeing that all chemicals present should be reported.

Summary of the issues:

In 1991, the EPA, Georgia EPD, and Hercules had a meeting in which they agreed to change the analytical method for toxaphene to report toxaphene and "some other product". The new method only reported toxaphene chemicals from the back half of the chromatogram. When toxaphene enters the environment as a mixture of over 670 chemicals, shifts in ratios of chemicals occurs by the most chlorinated loosing a chlorine atom or two and becoming the persistent form that appears in large quantities in the front half of the chromatogram. In 1997, the analytical method was changed further by eliminating any toxaphene chemicals not present in the same ratio as the calibration standard, further excluding toxaphene chemicals from quantification and reporting. The EPA OIG found these analytical method changes made by EPA Region 4 inappropriate. EPA Region 4 responded by developing another method that only measures 3 toxaphene chemicals (only found after people or fish metabolize the chemicals). This method would report none or ~3% of the toxaphene present. The EPA OIG said not to use the method and further stated that the Hp-Sed and Hx-Sed (toxaphene with 6 and 7 chlorines, which are the ones present in large amounts) should be reported. EPA Region 4 has steadfastly refused to report these toxaphene chemicals that are present in the largest amounts in defiance of the EPA OIG. (Under the Hercules Patent, toxaphene includes all chlorinated camphene with 3 to 10 chlorines attached)

At the Hercules 009 Landfill Superfund Site, a toxaphene cleanup level was set based upon the assumption that the other toxaphene manufacturing waste chemicals such as dioxin would be cleaned up to safe level. By not reporting all toxaphene present, other chemicals will not be cleaned up.

The EPA OIG use the example from our community where 56 fish samples from Terry Creek were analyzed by the inappropriate method and no toxaphene was reported in any sample. When re-analyzed by Negative Ion Mass Spectroscopy (NIMS), the fish had up to 26 ppm, or 56 times the EPA "Do Not Eat" level. Obviously, the inappropriate method is a health threat to all in our community and re-testing is needed. A similar situation could be occurring at Altama Elementary School, but like Terry Creek we will only know after appropriate testing is conducted.

EPA Region 4, Georgia EPD, and Hercules are united in their effort to keep all toxaphene chemicals being from being reported. The EPA's presentation to the Board of Education went one step further and declared, "...toxaphene breakdown products in soil do not pose a human health risk." The EPA did not produce any studies or data to support their contention that a poison and carcinogen do not pose a human health risk, but there are numerous studies to the contrary that are discussed in the Agency for Toxic Substance and Disease Registry (ATSDR) Toxicological Profile for Toxaphene. Furthermore, the EPA OIG interviewed the ATSDR toxicologist whom estimated only 10% of the toxaphene present was being reported.

Toxaphene is present in our community up to 8% in soils (yes, that is percent, or 88,000 ppm). Around 2-3 million pounds of toxaphene were released into our estuary. Four toxic sites have not been investigated or cleaned up that contain toxaphene.

EPA Region 4 has made a decision to continue to NOT report all chemicals present and declare toxaphene does not pose a health risk, even when all the chemicals present has not been determined. The GEC would like to resolve this situation in cooperation with the Glynn County BOE in a manner that does not alarm parents or children.

The Glynn County BOE needs to be satisfied that chemicals have not been left on school property, sufficient information is available to conduct drainage ditch maintenance activities without recontamination, and school property is not encumbered by chemical contamination.

The GEC is providing the following information in the form of a rebuttal to the EPA's presentation to the BOE. Please do not hesitate to ask if you need clarification or documents cited.

- **Slide: Removal and Testing...** There were two removal actions on school property. The one that extended along the ditch and to the playground was not included by EPA Region 4. Contrary to the contentions of the EPA, toxaphene contamination was found in 1995 up to and abutting the school playground, which the GEC is cognoscente and a factor in our request for retesting the school (See Attachment A). School property was tested after the removal action and levels up to 84 ppm remained. Notable is that the EPA presentation excluded this area that extends to the playground from the removal action presented to the BOE, which further emphasizes the need for retesting the school. It is unknown why EPA Region 4 would withhold information about the removal action and the extent of contamination on school property.

- **Slide: Sampling and Analysis...** 1.) EPA claims sampling of the school yard is not part of Superfund or the Superfund Site, but the EPA has this data as part of the Site record, as indicated by being part of the presentation, and the EPA actually tested the soil (See Attachment B).

2.) The EPA contends that in 1993, there was no method for weathered toxaphene, which is incorrect. EPA Method 8080 at the time provided for reporting "total toxaphene" or "apparent toxaphene". EPA Region 4, Georgia EPD, and Hercules changed this analytical method through an agreement in 1991 to reporting toxaphene and "some other product". The analytical method developed was called the "Toxaphene Task Force" (TTF) method, and after further changes in 1997 called the "Hercules Protocol". The OIG called the method EPA (Region 4) Method 8081. At the meeting in 1991 where the agreement was struck between EPA Region 4, Georgia EPD, and Hercules, all parties agreed that they had previously tested for apparent toxaphene that reports all chlorinated camphene present, including what is now called "degraded" toxaphene, which is the same as toxaphene manufactured but now present in different amounts of the individual chemical components.

The EPA OIG discussed the changes made to EPA Method 8081 by EPA Region 4 and how toxaphene in soil was underestimated, and out rightly not reported when known to be present.

> "However, EPA (Region 4) Method 8081 is not effective for detecting degraded toxaphene (i.e., "weathered" toxaphene) in environmental samples (e.g., soil, water, fish). For demonstration purposes, chromatogram 3A below is a known chromatogram of toxaphene degradation products in soils. When chromatogram 3A is compared by EPA Method 8081's identification criteria for technical toxaphene, chromatogram 3A obviously does not have the 22 same late eluding peak profile (i.e., the peaks after 29 minutes) as the technical toxaphene standard. **Therefore, a match is not made and the presence of toxaphene is not reported by the laboratory, even though specific toxaphene congeners (e.g., Hx-Sed and Hp-Sed) are known to be present.** This example demonstrates the manner in which EPA (Region 4) Method 8081 fails to detect toxaphene degradation products (i.e.,"weathered" toxaphene or individual toxaphene congeners) in environmental samples."

The OIG's observation that toxaphene was present when none was reported by the TTF and Hercules Protocol methods is the same conclusion other studies have reached and confirmed though analysis. The OIG suggested that the observed compounds might be "toxaphene breakdown products", but many of the prominent chlorinated camphene (PCC) found in the front half of the chromatogram are associated with unmodified toxaphene or PCC as manufactured by Hercules.[i],[i],[i],[i]

The EPA Region 4 chemist, who also participated in the development of the TTF method, noted that the "latter peaks" in samples were decreased and the "early peaks" were increased in environmental samples from Brunswick, and that the TTF method may seriously underestimate the true concentration of toxaphene.[i],[i] The Georgia Environmental Protection Division chemist that participated in development of the TTF method noted that unknown peaks not quantified may have been toxaphene related and the total area method was not used when the TTF method was applied.[i] EPA Method 8081 requires that results report total toxaphene present, which was not done at Altama Elementary School. It is very unusual that analysis is conducted and chemical compounds present are not reported, as with the TTF method. Appropriate analytical methods, intended to protect human health and the environment, include the reporting of unidentified compounds when they are encountered.

Dr. R. Kevin Pegg, the community's Technical Advisor provided by an EPA Grant, summarized the analytical methods used in Glynn County, Georgia as follows:

Total Area Method

This is the basic method required by the US EPA for chemicals with multiple congeners. It detects technical, weathered and biological grades of toxaphene, as well as the off-grade product and manufacturing residue forms. Basically, all of the possible toxaphene chemicals are detected and added together to quantify total toxaphene. This method was not used by the EPA in Brunswick, Georgia, but is used at other EPA sites in the United States and by other governments and researchers around the world.

Toxaphene Task Force Method

This method was developed by EPA Region 4 in Atlanta, Georgia, with Hercules Inc., and the State of Georgia. While gas chromatography is still used, only a few of the chemicals specific for technical toxaphene are used in the analysis. Even if other toxaphene chemical congeners are present, they are ignored. The toxaphene task force method (referred to as EPA Method 8081) detects technical grade toxaphene as well as the total area method; however 8081 does not detect all off-grade products, does not detect some forms of manufacturing residue toxaphene, and can only detect weathered toxaphene in the first few years after placing in the environment. The TTF method does not detect toxaphene after it has been in the environment for

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several years, and it does not detect biological toxaphene. The TTF method is apparently used only in Glynn County Georgia and nowhere else in the world. The method is not recognized by other governments or by researchers as a useful method because it under-reports the actual toxaphene concentration.

GC negative ion mass spectroscopy

This technique, called the NIMS method, can detect all forms of toxaphene and is a widely respected method with a high degree of scientific merit regarding the interpretation of results. It is especially useful for detecting biological forms of toxaphene accumulation.

- Slide: Altama Elementary Sampling Results... The three congener method the OIG warned not to use is presented under Simon/Manning. The EPA OIG noted:

> "The other toxaphene degradation congeners of principal concern for the human health evaluation (e-g., p26, p50, and p62) would only become the dominant congeners upon the subsequent metabolism of this microbially degraded toxaphene (e.g., Hx-Sed and Hp-Sed) by higher organisms (e.g., fish or humans). Therefore, if the EPA or PRP (Potentially Responsible Parties) test a site for only the p26, p50, and p62 congeners, the EPA or PRP will significantly under estimate the amount of contamination by toxaphene degradation products at the site."

It is notable that EPA Region 4 continues to advocate for toxaphene analytical methods that will underestimate or fail to detect the chemicals of concern present. Obviously, the toxaphene on school property and in the water has not been degraded by the metabolism of fish or humans. EPA Region 4's introduction of Simon and Manning PRGs is meaningless to the discussion and meant to confuse the BOE. This is EPA Region 4 implementing a method the OIG specifically said not to because it would under estimate the amount present.

- Slide: Drainage Ditch ... The EPA has never explained how toxaphene crossed a 6 foot deep ditch and went hundreds of feet onto school property. As noted previously, there were two removal actions on school property. The one that extended along the ditch and to the playground was not included by the EPA. Contrary to the contentions of the EPA, toxaphene contamination was found in 1995 up to and abutting the school playground, which the GEC is cognoscente and a factor in our request for retesting the school (See Attachment A). School property was tested after the removal action and levels up to 84 ppm remained. Notable is that the EPA presentation excluded this area from the removal action presented to the BOE, which further emphasizes the need for retesting the school. It is unknown why EPA Region 4 would withhold information about the removal action and the extent of contamination on school property. The OIG interviewed two experts that independently estimated the inappropriate method used on school property would report around 10% of the toxaphene present, which leaves doubt about the protectiveness of the cleanup.

- Slide: 2005 Office of Inspector... EPA Region 4 made a gross misrepresentation of the OIG findings, and attempted to re-write history the way EPA Region 4 wants it to read. The GEC presented 128 concerns about the remediation of the Hercules 009 Landfill Superfund Site. The OIG addressed only 3 of the concerns. One of the 128 the GEC did raise concerns about was retesting areas previously tested by the inappropriate method. As noted previously, the EPA OIG advocated for testing soil when there were doubts about the testing conducted previously.

As EPA Region 4 noted, risks were to be evaluated, which cannot be completed without identifying chemicals of concern present.

The EPA OIG noted:

> "When toxaphene contamination is suspected, the groundwater and **soil** analyses should test for Hx-Sed and Hp-Sed because they would be the dominant toxaphene degradation products."
>
> "In my opinion, the published science is clear that the dominant congeners generated by the microbial breakdown of technical toxaphene in **soil** are Hx-Sed and Hp-Sed with the other toxaphene congeners being present at much lower levels. Therefore, if the EPA or the potentially responsible party (PRP) are testing to determine the nature and extent of the contamination at a site by toxaphene degradation products, the dominant toxaphene congeners in the **soil** or groundwater samples will be Hx-Sed and Hp-Sed."

EPA Region 4's contention that the OIG focused on only water appears to be intentionally misleading. The OIG noted extensively that EPA Region 4 was steadfast in their refusal to report all chemicals present and has engaged in reporting only some of the chemicals known to be present since 1993, which is prior to the testing of Altama Elementary school by the three parties (EPA Region 4, Georgia EPD, and Hercules) that developed the inappropriate method.

The OIG noted:

> "Unfortunately, EPA Region IV and I continue to disagree as to whether environmental testing for toxaphene degradation products by the GC/NIMS methodology should include Hx-Sed and Hp-Sed. Region IV does not agree with the OIG's stated opinion that Hp-Sed and Hx-Sed congeners need to be definitively determined in environmental testing for toxaphene degradation products."

- Slide: 2006 Groundwater... Again, EPA is implementing Simon & Manning, even though the OIG said it would underestimate amount present.

- Slide: Toxaphene Exposure... EPA Region 4 presented irrelevant information about toxaphene exposure in the Netherlands. Unlike the Netherlands, the school is sitting next to a Superfund Site containing the manufacturing wastes from the production of toxaphene with documented releases and failures to control migration to drainage ditches and school property. Furthermore Toxaphene was manufactured in Brunswick and the wastes, including dioxin, were disposed in the landfill. It is all the manufacturing waste chemicals that are a concern, and not just technical toxaphene. The landfill contains toxaphene manufacturing wastes and off-grade product that will have much different chemicals ratios and contaminants than the toxaphene pesticide sold for agricultural use. For these reasons, it is imperative to test for and report all chemicals present.

- Slide: Re-evaluation of Site Risks 1.) EPA Region 4 recalculated risk from toxaphene and published it as Simon & Manning. The OIG explicitly said the calculations should be provided. The GEC asked for the calculations from EPA Region 4 and they could not produce the calculations, nor would the authors. The GEC has this correspondence from EPA Region 4.

2.) EPA Region 4 claims prevalent congeners (Hx-Sed and Hp-Sed, or toxaphene with 6 and 7 chlorines attached) are of lesser concern because they are eliminated from the body quickly. No data in support was presented, but there is a lot to the contrary.

3.) EPA claims there is no screening criteria for prevalent congeners, which is incorrect. Prior to the meeting in 1991 when an agreement was made to change EPA Method 8081, the parties agreed previous testing did report "total" or "apparent toxaphene," which did report all toxaphene chemicals present. Furthermore, the method advocated by the OIG, Gas Chromatography - Negative Ion Mass Spectroscopy (GC-NIMS) has been used in Glynn County for fish and water since at least 2000 and has been identifying and quantifying the very chemicals EPA Region 4 claims there are no screening criteria. Under the Performance Standards Act, scientifically accepted and peer reviewed analytical methods can be used by the EPA. In the case of NIMS, the EPA has been using the method for over 20 years and the results extensively published in scientific peer reviewed journals. EPA Region 4 inferred that since research is being conducted about analytical methods that testing cannot be done at the school, which is misleading and outright wrong. The presentation concerning risks appears to be intended to baffle and confuse the BOE concerning the OIG findings, recommendations, and appropriate methods to test the school to definitively determine risk to students.

- Slide: Region 4 Response... EPA Region 4 claims weathered toxaphene poses less risk, but produced no data in support. Available science contradicts EPA Region 4's position, and identifies the chemicals being excluded and not reported as being MORE toxic than the technical toxaphene mixture. The ATSDR Toxicological profile for Toxaphene states:

> "Toxaphene components A and B have been isolated and found to possess toxicity that is 6 and 14 times greater, respectively, than the technical toxaphene mixture as measured by comparing intraperitoneal LD50 values in mice (Casida et al. 1974). Toxicant A has been identified as a mixture of 2,2,5-endo,6-exo,8,8,9, 10-octachlorobomane and 2,2,5-endo,6-exo,8,9,9,10- octachlorobomane (Matsumura et al. 1975; Turner et al. 1975) and **toxicant B has been identified as 2,2,5- endo,6-exo,8,9, 10-heptachlorobomane** (Casida et al. 1974). **It has further been determined that toxicant B and four of its derivatives, each with an additional chlorine atom at position 3-exo,8,9, or 10, may be responsible for the bulk of toxaphene's acute toxicity** (Saleh et al. 1977)."

Important to note is that the EPA OIG identified toxicant B, Hp-Sed, as being one of the most prevalent chemicals present. Attachment C identifies the congeners that are accepted as being technical toxaphene, which do include the very chemicals EPA Region 4 continues to advocate for not reporting, even when they are known to be present. As Attachment C demonstrates, EPA Region 4 has arbitrarily excluded chemical components of the technical toxaphene mixture with 6 and 7 chlorines attached (Hp-Sed and Hx-Sed), which are the chemical components identified by the OIG as most prevalent, and as the most toxic by ATSDR.

Contrary to the contentions of EPA Region 4 that these chemicals pose less risk and lesser concern, ATSDR found:

> "Information on the toxicities of components in the original mixtures is limited to perhaps 10 congeners, the most familiar being the appreciably toxic and persistent toxicant A and toxicant B."

The ATSDR Toxicological profile for Toxaphene states the following about the toxicological effects of toxaphene on children:

> "Pregnant women, fetuses, nursing infants, and very young children may be at greater risk of adverse health effects from pesticide exposure than the general population (Calabrese 1978). Exposure to organochlorine insecticides, such as toxaphene, may adversely affect reproductive physiology (i.e., hormonal balance) in certain women (Calabrese 1978). Embryos, fetuses, and neonates up to age 2-3 months may be at increased risk of adverse effects following pesticide exposure because their enzyme detoxification systems are immature (Calabrese 1978). Animal studies suggest that detoxification of the toxaphene mixture may be less efficient in the immature human than the metabolism and detoxification of the single components such as toxicant A or B (Olson et al. 1980). Infants and children are especially susceptible to immunosuppression because their immune systems do not reach maturity until 10-12 years of age (Calabrese 1978)."
>
> "Animal studies suggest that detoxification of the toxaphene mixture may be more inefficient in immature animals and possibly also in children than the metabolism and detoxification of the single components such as toxicant A or B."
>
> "Humans living in areas surrounding hazardous waste sites may be exposed to toxaphene via ingestion of contaminated water or even ingestion of soil, particularly by children. Inhalation exposure to toxaphene via volatilization from contaminated water or soil may also occur."
>
> "Subsets of the human population that may be unusually susceptible to the toxic effects of toxaphene include pregnant women, their fetuses, nursing babies, young children, people with neurologic diseases (particularly convulsive disorders), and individuals with protein-deficient diets. Others at increased risk include people with hepatic, cardiac, renal, or respiratory diseases, those with immune system suppression, and those ingesting alcohol or consuming therapeutic or illicit drugs."

Slide: Conclusions... 1.) EPA Region 4, based upon the use of previous testing from 1993 the OIG found inappropriate, concluded there is no site related impact. Relying on an analytical method known to exclude the chemicals that are most prevalent and most toxic underscores EPA Region 4's effort to prevent testing that will report all chemicals present.

2.) EPA Region 4's claim that toxaphene does not poses a health risk is not supported by data but rather a flimsy argument that there is no risk to students if unknown chemicals are present. Risk cannot be determined until the school is tested and all chemicals present are reported.

In closing, the cleanup of the Hercules 009 Landfill Superfund Site was based upon cleaning up toxaphene to 0.25 ppm would also cleanup the other chemicals such as dioxin, a waste product from the manufacture of toxaphene. If all the toxaphene chemicals are not reported, the other toxic chemicals in the toxaphene manufacturing wastes will not be cleaned up. The first step in protecting children is to report all chemicals present on Altama Elementary School property. In addition, sufficient information should be collected to assure the Glynn

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County BOE that drainage ditch maintenance can be conducted without recontamination, and school property is not encumbered by chemical contamination.

Attachment J

Review of EPA's January 29, 2008, Presentation

by Dr. R. Kevin Pegg

At the request of the Glynn Environmental Coalition I reviewed the recent January 29, 2008 EPA PowerPoint presentation **to the Glynn County Board of Education**. There are factual errors and scientific inaccuracies contained within this presentation.

First, "toxaphene" is a trade name for a toxic and carcinogenic mixture of chlorinated organic chemicals. Toxaphene was never a chemically defined preparation. Camphene from pine stumps was chlorinated until a toxic endpoint was reached using a fly bioassay—a test to see how many flies died in a fixed period of time with a known quantity of toxaphene. Off-grade product with mixed results for fly killing was stored on the Hercules site for many years, or placed into the 009 landfill. Contamination outside of the 009 landfill repository cells was proven beyond doubt in numerous studies conducted during the mid-1990's. Toxaphene was found along the transportation route to the landfill, in the neighborhood adjacent the landfill, on the school grounds adjacent the landfill, in the drainage ditch separating the landfill from the school, and outside of the containment cells on landfill grounds.

All of the available science shows beyond doubt that toxaphene, including technical grade and so-called "weathered" toxaphene, is a biocide (kills across species lines), is mutagenic, and causes cancer in laboratory rodents. These studies have been replicated in numerous laboratories with appropriate scientific controls and are not in dispute. However, there are very few scientific studies showing which of the many chemicals in toxaphene are most toxic, most mutagenic, or most carcinogenic. When there are few peer–reviewed and replicated studies proving safety both the Environmental Protection Agency (EPA) and the Agency for Toxic Substances Disease Registry (ATSDR) mandate cleaning up the environment using the most conservative levels (the lowest amounts) of the target chemical. All Federal agencies involved in regulating foreign substances-- The Food and Drug Administration (FDA), United States Department of Agriculture, and Occupational Safety and Health Administration (OSHA) also use the common-sense and prudent approach of erring on the side of caution when it comes to complex chemicals.

Federal guidelines mandate that potential environmental exposure pathways to toxic chemicals must be defined. Pathways include exposure through air (volatile chemicals and small particles), surface or groundwater (soluble chemicals), or soil. Extensive toxaphene contamination was found in the soil of the elementary school adjacent the 009 Landfill Superfund Site. Further, there was ample evidence of human use (trails, trash) throughout the contaminated areas. Contemporaneous documents defined both past landfill site operations and contaminated spoil piles from the stream placed on school property as sources of the toxaphene on school property. It is a scientific fact that a completed exposure pathway for soil did exist on school grounds. Region 4 EPA's assertion that only groundwater exposure at this site is relevant is not consistent with the site history. Note that the slides entitled "2006 Groundwater Sampling" and "Toxaphene Exposure Risks" are entirely irrelevant for any discussion of a soil pathway. It is unclear why EPA is asserting groundwater data in regard to soil sampling issues, there is no logical reason for making a claim for soil safety based on water.

All of the available analytical science shows that toxaphene is a straightforward chemical mixture to analyze and characterize. The EPA has had in place, for decades, scientific methods for quantifying multi-component mixtures. Toxaphene can easily be quantified using gas chromatography with a variety of detectors. These instruments are common to nearly every laboratory, and the techniques are straightforward. Toxaphene is routinely quantified using this standard equipment and standard EPA methods in laboratories around the country and around the world. There is no scientific rationale for a special toxaphene method just to monitor toxaphene in Glynn County, Georgia. EPA's assertion that no method existed in 1993 to test for "weathered" toxaphene is nonfactual. Standard EPA methods would have quantified toxaphene at this site in 1993, and were in use at that time at other sites with far less toxaphene.

Risk modeling is a well-established science. When calculating risk the nature of the chemical is taken into consideration, the amount of chemical exposure—concentration of chemical and duration—is factored into the equation, and toxicology effects from animal and human exposure all are assigned values. These models are then placed into the public domain so that other toxicologists can validate the findings. There currently are mathematical risk assessment models for assessing toxaphene risk. EPA asserts in a slide titled "Re-evaluation of Site Risks" that "EPA Region 4 conducted a re-analysis of European toxicity data and determined that weathered toxaphene breakdown products are less toxic than technical toxaphene." If these models are published then the reference should be given, especially since Region 4 EPA is not a third party to this controversy. Region 4 actually created this controversy by using unscientific methodology, which cannot be set aside with non-reviewed internal studies and opinions. No scientist would accept Region 4's statement at face value without seeing EPA's model entire mathematical model used for the reassessment.

There is no scientific support for Region 4 EPA's claims that toxaphene in Brunswick, Georgia:

- requires special methods for detection;
- does not require monitoring; and,
- is proven safe based on Region 4's reassessment.

Further, the opinions expressed by EPA Region 4 are contrary to agency guidelines. Unlike other parts of the country, and the world, Glynn County-- likely one of the most toxaphene contaminated areas anywhere-- has not received the benefit of simple scientific analyses for toxaphene in soil. It is reasonable to expect Region 4 to follow the order of their own Inspector General to test the vicinity of the landfill with the EPA's validated methods, rather than rely on data using a discredited technique.

R. Kevin Pegg, Ph.D.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 31 2006

OFFICE OF
INSPECTOR GENERAL

MEMORANDUM

SUBJECT: OIG Ombudsman Report 2005-P-00022
Appropriate Testing and Timely Reporting Are Needed at the
Hercules 009 Landfill Superfund Site, Brunswick, Georgia

FROM: Paul D. McKechnie Paul D. McKechnie
Director of Public Liaison
Office of Congressional and Public Liaison

TO: J. I. Palmer, Jr.
Regional Administrator
Region 4

We have evaluated your final response dated June 20, 2006, to the subject report, as well as the related attachments (such as the second 5-year report dated June 2006) and additional documents provided by members of your staff. The latter included the article by Ted Simon and Randall Manning, *Development of a reference dose for the persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion,* and the results of recent tests of the groundwater at the Hercules 009 Landfill site. The associated documents were reviewed by a chemist currently on our staff and by the subject matter expert who worked on the assignment who is now employed by another Federal agency. We also took into consideration the comments provided to us on September 7 and October 10, 2006, by the Glynn Environmental Coalition and its consultants.

We believe additional research is necessary to increase the confidence in Region IV's assessment on the human health risks posed by toxaphene degradation products, however, we are closing this report because you have adequately addressed the recommendations we made. Our basis for reaching this conclusion is described in the attached letter dated October 23, 2006. As this letter points out, for scientific and regulatory transparency, you should provide a detailed description of how the preliminary remediation goals (PRGs) for weathered toxaphene were calculated. Some other key points related to your response that are detailed in the letter are:

- The PRGs Region IV developed for weathered toxaphene, not the drinking water program's maximum contaminant level for technical toxaphene, should now be used to evaluate the human health risk.

- When toxaphene contamination is suspected, the groundwater and soil analyses should test for Hx-Sed and Hp-Sed because they would be the dominant toxaphene degradation products.

- The analysis performed on the groundwater samples collected at the Hercules 009 Landfill in March 2006 (not March 2005) included quality controls sufficient to ensure the results can be accurately interpreted.

As we noted in Report 2006-P-00007 dated December 16, 2005, *More Information Is Needed On Toxaphene Degradation Products,* additional research and scientific study is needed to assess the health risk posed by the human exposure to toxaphene degradation products. We urge you to work closely with the Office of Research and Development as they prepare their multi-year research plan, so it includes toxaphene degradation products. Similarly, we believe the Office of Research and Development and the Office of Solid Waste and Emergency Response will need help from you to develop the analytical method using negative ion mass spectroscopy.

If you or your staff has any questions regarding this matter, please contact me at 617-918-1471 or Christine Baughman, the Project Manager, at 202-566-2902.

Attachment

cc: Susan Bodine, Assistant Administrator for Solid Waste and Emergency Response
George Gray, Assistant Administrator for Research and Development
Benjamin Grumbles, Assistant Administrator for Water
Stephanie Lankford, Region 4 Audit Liaison
Johnsie Webster, OSWER Audit Liaison
Cheryl Varkalis, ORD Audit Liaison
Mike Mason, OW Audit Liaison
Laurie Dubriel, Special Assistant to the Administrator
Winston A. Smith, Director, Waste Management Division, Region 4
Leo Francendese, Remedial Project Manager, Region 4
Daniel Parshley, Project Manager, Glynn Environmental Coalition

October 31, 2006

Paul Mckechnie
Director Public Liaison/Ombudsman
Environmental Protection Agency
Office of Inspector General
Office of Congressional and Public Liaison
1200 Pennsylvania, Ave, N.W. (2491T)
Washington, D.C. 20460

Dear Paul,

At your request, I am providing you my technical opinion on EPA Region IV's final response (Dated June 20, 2006) to the Ombudsman's Recommendations 2.1 and 2.2 in the Report 2005-P-00022 (dated Sept. 26, 2005). The Ombudsman Report 2005-P-00022 concerned EPA Region IV's assessment, during the second 5-Year Review, of the public health risk posed by degraded toxaphene at the Hercules 009 Landfill Superfund site. As a former EPA/OIG Environmental Scientist on your staff, I served as the subject matter expert for each of the Ombudsman reports on toxaphene (i.e., Reports 2005-P-00022 and 2006-P-00007). This experience provides me with an in depth knowledge of the subject and I present my observations and findings for your consideration. Since I am no longer an EPA employee, this review and subsequent development of my technical opinion were performed pro bono.

I received and reviewed the following five documents to develop my technical opinion on Region IV's final response to the OIG's Recommendations 2.1 and 2.2 in Report 2005-P-00022:

- [EPA Region IV's] Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia Assignment 2004-124* (dated June 20, 2006).

- The Hercules 009 Landfill April 2006 GC/ECD and GC/ECNI-MS-SIM ground water testing results performed by Pace Analytical Laboratories on behalf of Hercules Incorporated (dated June 15, 2006).

- Ted Simon, Randall Manning; Development of a reference dose for persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion. Regulatory Toxicology and Pharmacology, Vol. 44 (2006), pages 268-281.

- Comment from the Glynn Environmental Coalition on the June 20, 2006, EPA Region 4, Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (dated September 7, 2006) including the enclosed attachments from R. Kevin Pegg, Ph.D. and Kathleen Burns, Ph.D.

- Comments to OIG on Hercules 009 Superfund Reports by Jennifer Sass, Ph.D. (dated October 10, 2006).

The purpose of a 5-year review is to assess if the remedy is still protective in light of any new science or site information that has occurred since the last assessment. Since toxaphene is well known in the scientific literature to degrade in the environment, the 5-year review needs to determine the amount of exposure (if any) and the resulting risk to the public from degraded toxaphene from the site. This is accomplished by accurately measuring the amount of degraded toxaphene in the groundwater at the site, by determining if any of the contaminated toxaphene groundwater has left the site, and by determining the human health risk posed by any degraded toxaphene that might have left the site.

Evaluation of Hercules 009 Groundwater Testing

The second 5-year review of the Hercules 009 site used the Gas Chromatography/Negative Ion Mass Spectrometry (GC/NIMS) method to determine the amount of degraded toxaphene in the groundwater. However, the March 2005 GC/NIMS groundwater results have several limitations:

- The test results do not positively identify individual toxaphene degradation congeners (i.e., through a mass spectrum or selective ion monitoring confirmation) or determine the amount of individual toxaphene degradation congeners (i.e., p26, p50, Hx-Sed, Hp-Sed, etc.) present in the groundwater. This severely limits the ability to technically interpret the results with an acceptable level of confidence.

- The Quality Control used in March 2005 did not incorporate a Laboratory Control Sample (LCS) that contained known amounts of individual toxaphene degradation congeners. Therefore, without LCS results for individual congeners, the ability of the method to detect and confirm the presence of individual toxaphene congeners is questionable.

However, the GC/NIMS groundwater samples taken subsequently at the Hercules 009 Landfill site in April 2006 can be accurately interpreted. These GC/NIMS groundwater sample results are the type of testing the OIG/Ombudsman has been requesting in order to accurately measure the amount of degraded toxaphene in the groundwater at the site and to determine if any of the contaminated toxaphene groundwater has left the site.

The GC/NIMS groundwater samples taken at the Hercules 009 Landfill site in April 2006 positively identify (i.e., by Selective Ion Monitoring (SIM)) and quantitate the following eight individual toxaphene congeners: p26, p41, p40, p44, p50, p62, Hx-Sed, and Hp-Sed. In reviewing the results, the following observations and findings can be made:

- The method blank results show no laboratory contamination of toxaphene congeners.

The Laboratory Control Sample (LCS) and LCS duplicate recoveries are from 63% to 95% for the eight individual congeners and show that the GC/NIMS analysis is performing well for the detection of these eight individual toxaphene congeners. The LCS quality control results document the method's ability to detect individual toxaphene congeners in samples reliably.

- Matrix Spike (MS) and Matrix Spike Duplicate (MSD) quality control sample recoveries are from 60% to 96% for the eight individual congeners and show that the groundwater matrix does not interfere with the analysis.

- Only two groundwater monitoring wells, N-06SR and N-11, were found to have degraded toxaphene congeners significantly above the Level of Quantitation (LOQ) (See Table 1). These results are consistent with the published science on the degradation of technical toxaphene. The dominant congeners generated by the microbial breakdown of technical toxaphene are Hx-Sed and Hp-Sed with the other toxaphene congeners being present at much lower levels. The other toxaphene degradation congeners of concern (i.e., p26, p40, p41, p44, p50, and p62) would only become the dominant congeners upon the subsequent metabolism of this microbially degraded toxaphene (e.g., Hx-Sed and Hp-Sed) by higher organisms (e.g., fish or humans). The groundwater results for monitoring wells N-06SR and N-11 show that the technical toxaphene has degraded and that Hx-Sed and Hp-Sed are the dominant congeners with the other toxaphene congeners being present at much lower levels.

Ground Water Well	Hx-Sed (ppb)	Hp-Sed (ppb)	p26 (ppb)	p40 (ppb)	p41 (ppb)
N-06SR	0.186	0.128	0.009	≤0.005	0.005
N-06SR Duplicate	0.156	0.116	0.009	0.034	0.005
N-11	0.133	0.095	≤0.005	0.012	≤0.005
N-14S	≤0.005	≤0.005	≤0.005	≤0.005	<0.005
N-14D	<0.005	<0.005	<0.005	<0.005	<0.005

Table 1: Subset of the April 2006 GC/NIMS Groundwater Results

- The groundwater results for the furthest down-gradient monitoring well, N-14, did not detect toxaphene degradation products above the LOQ (See Table 1). This indicates that the toxaphene degradation products found in groundwater wells N-06SR and N-11 have not left site.

OIG Recommendation 2.1

The OIG recommendation to the EPA Region IV was to use the GC/NIMS to definitively determine if toxaphene breakdown products are present in and around the surrounding groundwater at the Hercules 009 Landfill site, and (if so) in what amounts.

EPA Region 4 has implemented the OIG Recommendation 2.1 with the April 2006 GC/NIMS groundwater testing at the Hercules 009 Landfill. These groundwater results definitively show that the technical toxaphene can and has degraded and that Hx-Sed and Hp-Sed (i.e., the microbial toxaphene breakdown products) are present at a maximum concentration of 0.186 ppb and 0.128 ppb, respectively. Several of the other toxaphene congeners (e.g., p26, p40, and p41) are also present, but at much lower levels. Since the April 2006 GC/NIMS groundwater results are consistent with the published science on the degradation of technical toxaphene and since the LCS and MS quality control results indicate that the GC/NIMS method was performing well, the April 2006 GC/NIMS groundwater results can be concluded to accurately characterize the site's groundwater conditions for toxaphene degradation products.

Unfortunately, EPA Region IV and I continue to disagree as to whether environmental testing for toxaphene degradation products by the GC/NIMS methodology should include Hx-Sed and Hp-Sed. Region IV does not agree with the OIG's stated opinion that Hp-Sed and Hx-Sed congeners need to be definitively determined in environmental testing for toxaphene degradation products (see Region IV Final Response cover memo, page 2; and Attachment C of the Region IV Final Response, page 38). In my opinion, the published science is clear that the dominant congeners generated by the microbial breakdown of technical toxaphene in soil are Hx-Sed and Hp-Sed with the other toxaphene congeners being present at much lower levels. Therefore, if the EPA or the potentially responsible party (PRP) are testing to determine the nature and extent of the contamination at a site by toxaphene degradation products, the dominant toxaphene congeners in the soil or groundwater samples will be Hx-Sed and Hp-Sed. The other toxaphene degradation congeners of principal concern for the human health evaluation (e.g., p26, p50, and p62) would only become the dominant congeners upon the subsequent metabolism of this microbially degraded toxaphene (e.g., Hx-Sed and Hp-Sed) by higher organisms (e.g., fish or humans). Therefore, if the EPA or PRP test a site for only the p26, p50, and p62 congeners, the EPA or PRP will significantly under estimate the amount of contamination by toxaphene degradation products at the site.

Furthermore, the EPA and/or the PRP need to monitor the groundwater at a site to insure that toxaphene contaminated groundwater is not leaving the site. Since Hx-Sed and Hp-Sed would be the dominant congeners in groundwater, how can EPA or the PRP monitor the groundwater contamination and determine if the contamination is leaving the site without monitoring for Hx-Sed and Hp-Sed? Furthermore, the additional cost to test for the Hx-Sed and Hp-Sed congeners in the GC/NIMS method is minimal (i.e., the cost of including the Hx-Sed and Hp-Sed in the calibration standards and spike solutions for the LCS and MS quality control samples). There is no practical or scientific reason to exclude Hx-Sed and Hp-Sed in the testing for contamination by toxaphene degradation products. Therefore, it is my opinion that it is imperative that the EPA-approved GC/NIMS method under development by the Office of Research and Development include Hx-Sed and Hp-Sed as target congeners in the method.

Evaluation of the Human Health Risk to Degraded Toxaphene

EPA Region IV Final Response (Cover Memo) compares the concentrations of toxaphene degradation products in the groundwater to the drinking water maximum contaminant level (MCL) of 3.0 ppb for technical toxaphene. The composition of the congeners present in technical toxaphene is distinctly different than the composition of the congeners found in degraded toxaphene. The composition of technical toxaphene is mostly comprised of the higher chlorinated level of boranes, while the degraded toxaphene is principally made of the lower chlorinated levels of boranes such as Hx-Sed, Hp-Sed, p26, p50 and p62, etc. Furthermore, since the last significant use of technical toxaphene was in 1982 and since technical toxaphene is known to degrade in the environment, the human population is no longer exposed to technical toxaphene, but is exposed to toxaphene degradation products. Therefore, the continued application of the drinking water MCL of 3.0 ppb for technical toxaphene in the risk assessment of toxaphene degradation products is scientifically inappropriate. For that matter, since the human population is and will no longer be exposed to technical toxaphene, the drinking water MCL of 3.0 ppb for technical toxaphene can be retired for the lack of an appropriate risk management application.

In response to the OIG Recommendation 2.2 to assess the risk to human health from the potential exposure to toxaphene breakdown products, EPA Region IV conducted a re-analysis of the European MATT (2000) toxicity data and developed a reference dose for weathered toxaphene. Ted Simon and Randall Manning published their findings in the following scientific journal: Regulatory Toxicology and Pharmacology, Vol. 44 (2006), pages 268-281. EPA Region IV states in their Final Response (See attachment B, page 2) that "… the Simon/Manning approach should be considered the best available science; therefore, the Region's reliance on this approach to assess the risk associated with this site is appropriate."

In my opinion, the Simon and Manning paper is significant in the field of scientific research into toxaphene because it is the first published paper that quantifies the risk of weathered toxaphene. The authors make a number of key determinations (e.g., weathered toxaphene's mode of action is as a promoter, applied the unconventional use of a reference dose to a carcinogen, applied a uncertainty factor of a 100, etc.) whose application for calculating an acceptable exposure limit to weathered toxaphene is open for debate and to further research and study within the scientific community. However, the Simon/Manning paper does represent the best and only available scientific information that quantifies the human health risk to weathered toxaphene for use in the second 5-year review of the Hercules 009 Landfill. Science is dynamic and continuously evolves as new information becomes available, so the Simon/Manning paper is not the last word on the issue, but represents the next step into the understanding of the amount of risk posed by weathered toxaphene. More scientific information should be available in five years to allow for a better estimate of the human health risk posed by weathered toxaphene for the next 5-review of the Hercules 009 Landfill in 2011.

EPA Region IV states in their Final Response (See attachment B, page 2) that "… the Simon/Manning approach should be considered the best available science; therefore, the Region's reliance on this approach to assess the risk associated with this site is appropriate." However, EPA Region IV does not use the Simon/Manning approach to assess the risk associated with this site. EPA compares the concentrations of toxaphene congeners in the groundwater to the drinking water MCL of 3.0 ppb. However, in my opinion, to be consistent with their statement on the Simon/Manning approach, EPA Region IV needs to evaluate the concentrations of toxaphene degradation products against the Preliminary Remediation Goals (PRGs) established in the Simon/Manning paper for ∑3PC and weather toxaphene of 0.03 ug/L and 0.6 ug/L, respectively (See Table 5 in the Simon and Manning paper). Unfortunately, the Simon/Manning paper does not show how the PRGs were calculated. Therefore, I cannot independently verify them (i.e., EPA Region IV should be required to provide a detailed description of how these PRGs were calculated for scientific and regulatory transparency). However, EPA Region IV clearly states that it is the "best available science." Thus, EPA Region IV should apply these PRGs to the assessment of the risks associated with weathered toxaphene at the Hercules 009 Landfill and other toxaphene contaminated Superfund sites in Region IV. In other words, the EPA Region IV should use the 0.6 ug/L PRG for weathered toxaphene (which is 5-fold more restrictive than the 3.0 ppb drinking water MCL being applied by the Region) to evaluate the concentrations of degraded toxaphene congeners found in the groundwater.

When the April 2006 GC/NIMS groundwater results for the Hercules 009 Landfill site are compared against the PRGs for ∑3PC and for weathered toxaphene, the concentration of the toxaphene degradation products do not exceed either PRG. The groundwater samples from monitoring well N-06SR contained the highest levels of toxaphene degradation products. Specifically, the groundwater sample and duplicate from N-06SR contained 0.328 ug/L and 0.320 ug/L of weathered toxaphene, respectively. Both results are below the 0.6 ug/L PRG for weathered toxaphene. Furthermore, the groundwater sample and duplicate from N-06SR contained 0.009 ug/L and 0.009 ug/L for ∑3PC, respectively. Both results are below the 0.030 ug/L PRG for ∑3PC. Therefore, the level of groundwater contamination by toxaphene degradation products at the Hercules 009 Landfill site does not exceed the preliminary remediation goals and does not pose a health risk to the community at these levels.

OIG Recommendation 2.2

The OIG recommendation to the EPA Region IV was to assess the risk to human health by exposure to toxaphene breakdown products.

EPA Region IV has met the OIG Recommendation 2.2 with the development and publication of the Simon and Manning paper and their development of the Preliminary Remediation Goals for ∑3PC and Weathered Toxaphene of 0.03 ug/L and 0.6 ug/L, respectively (See Table 5 in the Simon and Manning paper). However, the EPA Region IV should be required to provide a detailed description of how these PRGs were calculated for scientific and regulatory transparency.

Protectiveness Statement

Based on the April 2006 GC/NIMS groundwater results indicating that the toxaphene degradation products have not left the site through the groundwater and also based on the observation that the maximum concentration of toxaphene degradation products is below the PRGs for ∑3PC and weather toxaphene of 0.03 ug/L and 0.6 ug/L, respectively, I concur with the Regional findings of the second 5-year review that the Hercules 009 Landfill site remedy is protective of human health and the potential exposure pathways are under control in regard to the contaminant toxaphene and its degradation products.

Conclusion

The two Ombudsman reports on toxaphene have been influential in shifting the entrenched paradigm of the EPA and PRPs to perpetually test for technical toxaphene and subsequently evaluate the risk against the limits set for technical toxaphene. The Ombudsman's efforts have promoted the recognition that currently, toxaphene only exists in the environment in a degraded, weathered state and that the regulatory and scientific communities need to test for and assess the risk posed from human exposure to weathered toxaphene. Furthermore, the completion of the EPA-approved GC/NIMS method by the end of 2008 and the subsequent use of this method by EPA and PRPs will definitively determine the extent of degraded toxaphene contamination left in the environment from 32 years of heavy use as an insecticide.

Sincerely,

/s/
Michael Wilson
Former Environmental Scientist with the EPA/OIG

cc: Christine Baughman

Mr. STUPAK. Thank you, Mr. Parshley.

Ms. Kneiss, your testimony, please.

STATEMENT OF SHARON H. KNEISS, VICE PRESIDENT, PRODUCTS DIVISION, AMERICAN CHEMISTRY COUNCIL

Ms. KNEISS. Thank you, Mr. Chairman, and good afternoon. My name is Sharon Kneiss and I am the Vice President of the Products Division at the American Chemistry Council. I appreciate the opportunity to be here today to talk about a flawed EPA process used to revise a very important health effects value for a lifesaving chemical.

The process failings go directly to the integrity of the science at EPA. Fundamentally, if you don't have confidence in the process, you can't have confidence in the result. In this case, EPA's procedures on paper are appropriate. Had EPA followed them, we wouldn't be here today. This June, EPA revised the oral reference dose, or RfD, for deca bromodiphenyl ether, a crucial flame retardant. EPA's failure to follow its own processes has produced an RfD in which EPA itself says it has low confidence. If these shortcomings are widespread, they could seriously undermine the integrity of IRIS.

ACC represents the leading companies in the business of chemistry. We have worked hard over the last decade to improve the quality and reliability of IRIS. Deca BDE is the most studied flame retardant and is widely used to help prevent fires and slow their spread. A prime example of the difference that flame retardants make is the Air France airliner that skidded off the runway and burst into flames in Toronto in 2005. Ignition of the seats and other fabrics on the plane was delayed for those vital few minutes so that all 309 passengers and crew could escape safely. It is important to remember that the reliability of this scientific review is not a theoretical or an academic exercise but poses real human consequences.

Because EPA did not follow its own guidelines for peer review processes and study integrity, two major failures occurred in the deca assessment. First, EPA used a completely inappropriate study to set the reference dose. Second, EPA did not vet the panel properly and appointed a chair who had made numerous public statements indicating she had already made her mind up on the science and had taken sides. In relying on the Viberg study to set an RfD, EPA failed to uphold its own most important science processes. The study did not follow EPA's Good Laboratory Practices or EPA's study protocols. EPA's TSCA Office said the study's methodology had a fundamental flaw and its author repeatedly ignored requests for the study data. Both EPA and the European Union regulators have concluded that the Viberg study is not adequate for quantitative risk assessment, and yet EPA used it even though the National Academies of Science had already derived an RfD using top-quality studies conducted by the National Toxicology Program.

EPA also failed to follow its own peer review handbook which ACC and NGOs alike endorse. The handbook is clear that the choice of peer reviewers should be based primarily upon the reviewer's expertise and experience and that reviewers should be sufficiently broad and diverse to fairly represent a balanced range of technical points of view. The handbook also recognizes, however, that experts with a stake in the outcome and therefore a conflict or appearance issue may be the most knowledgeable and up-to-date experts but federal law prohibits EPA from using peer reviewers who either have current financial conflicts of interest or appear to lack impartiality. It says as a general rule, experts who have clearly taken sides may have an appearance of a lack of impartiality and should be avoided. The National Academies and NGO groups draw a similar line.

To ensure that EPA gets this difficult balancing act right, the peer review handbook recommends that EPA notify the public before a peer review panel is formed, so interested parties can nominate proposed reviewers and provide the public with the list of proposed reviewers, so interested parties can comment on their qualifications and potential sources of conflict or bias. EPA did neither of these things. The peer review panel's composition did not reflect a wide range of expertise and was chaired by an individual who had not been adequately vetted and appeared to have made up her mind. For example, she told one newspaper that there was no question in her mind that deca should be eliminated because it is a persistent toxin that accumulates in the food chain. She told another, we know enough to ban deca, we don't need to wait another 2 years and let it increase in the environment while we nail down every possible question we have.

With all these concerns surrounding the panel and its deliberations, we wrote and met with EPA to express our concerns. We did not ask that the chair be removed from the panel or argue that the scientific expertise was the basis for the disqualification from the peer review board. But at that late date, there really was no satisfactory way to undo the damage caused by these process failures. As a result, we were reduced to asking EPA to base its final toxicological review on data, opinions, and conclusions other than the chairperson's. EPA ultimately deleted the chair's statements from the peer review panel's report but the damage was done. EPA's attempt to unring the bell thus had no effect on the ultimate result and did not benefit ACC. EPA has set an RfD for deca that is three orders of magnitude lower than the best available science supports.

ACC thanks the subcommittee for shedding light on the numerous process failures involved in the deca reassessment. I would be happy to answer any questions you might have.

[The prepared statement of Ms. Kneiss follows:]

Statement of Sharon H. Kneiss
Vice President of Products Divisions
American Chemistry Council

Before the

House of Representatives
Committee on Energy & Commerce
Subcommittee on Oversight & Investigations

Regarding

"Science Under Siege: Scientific Integrity
at the Environmental Protection Agency"

September 18, 2008

Introduction

Good morning Chairman Stupak, Ranking Member Shimkus, and members of the Subcommittee. My name is Sharon Kneiss and I am the Vice President of Products Divisions at the American Chemistry Council. I appreciate the opportunity to testify today regarding the flawed process that EPA used recently to revise an important health effects value for a life-saving chemical manufactured by several ACC member companies.

At the outset, I'd like to emphasize how crucial the integrity of EPA's scientific processes is to the integrity of EPA's scientific databases. Fundamentally if you don't have confidence in the process, you can't have confidence in the result. In this case, EPA's stated procedures – on paper – are appropriate. In particular, its *Peer Review Handbook* is a clearly written summary of the principles that should govern an agency peer review. It lays out the criteria for selection of peer reviewers, and it also describes the process for making those selections. The *Handbook* recommends:

- soliciting nominations from stakeholders, and
- giving notice to stakeholders of proposed panelists, *before* the panel is constituted.

The *Handbook* adds that panel members should:

- include world class scientists, since expertise is paramount;
- be sufficiently diverse to fairly represent relevant perspectives and fields of knowledge;

- represent a balanced range of technically legitimate points of view;
- not have current financial conflicts; and -- importantly,
- be open minded and be able to take an impartial approach to data examination. This means that panelists should not have made statements or taken other actions that would lead a reasonable person to conclude they had 'taken sides' on the issue in question.

The National Academies and NGOs endorse these procedures. Had EPA *followed* them, we would not be here today.

This June, EPA concluded the process of revising the oral reference dose or "RfD" for decabromodiphenyl ether (deca-BDE), a crucial flame-retardant. The many ways in which EPA failed to follow its own processes for scientific standard-setting, have resulted in an RfD in which EPA itself says it has "low confidence." The process was seriously flawed and the credibility of the outcome was its victim. If these shortcomings are widespread, they could seriously undermine the transparency and integrity of the Integrated Risk Information System, or "IRIS," EPA's hugely influential database of health effects data and dose-response values. The hearing presents a timely and important opportunity to highlight and investigate these failings in EPA's processes and their potential consequences for the integrity of science at EPA.

Background

The American Chemistry Council is the trade association that represents the leading companies in the business of chemistry. Established over a century ago, ACC is committed to improved environmental, health and safety performance through its Responsible Care® program, common sense advocacy, and health and environmental research and product testing. The business of chemistry is a $664 billion enterprise and a key element of the nation's economy. It is one of the nation's largest exporters, accounting for ten cents out of every dollar in U.S. exports. A significant part of ACC's work over the last decade has been to improve the quality and reliability of IRIS. ACC initiated and has actively supported bipartisan and successful efforts to increase the financial and personnel resources available to IRIS, without any quid pro quo or guarantee. ACC members are also among the nation's largest investors in scientific research and development. Through ACC's Long-Range Research Initiative and several voluntary testing programs, they have contributed tremendous amounts of technical expertise and experimental data to understanding and progress in the fields of toxicology and risk assessment that underlie the IRIS effort.

Deca-BDE is the most studied flame retardant on the market, having been the subject of an extensive 10-year evaluation by the European Union, as well as other major studies performed by the US EPA and the National Academy of Sciences, and has been found to present no significant risks to human health or the environment. Deca-BDE is used in plastics for electrical and electronic equipment, in the automotive and aviation industry, and in construction and building projects. It is also used as a flame retardant in furniture applications to comply with fire safety standards. Fabric and upholstery treated with flame retardants can help prevent fires from starting and can slow the spread of fires that have already ignited. Escape times can be up to 15 times longer when flame retardants are present, providing increased survival chances for those in close proximity to fire. A prime example is the Air France jet that skidded off the runway in Toronto in 2005 and burst into flames. The flame retardant materials used in the airplane's construction were credited with providing the extended escape time needed for all 309 passengers and crew to escape. Thus, it is important to remember the reliability of this scientific review is not an academic exercise, but poses real risk/risk tradeoffs involving human lives.

EPA's Flawed Process for Revising the Deca-BDE Oral Reference Dose

EPA's recent health assessment of deca-BDE is the story of important scientific and due process procedures that were not followed and the resulting adverse consequences for the integrity and transparency of EPA's scientific resources and for the public that relies on them. For the record, ACC also notes that industry did not benefit from the ultimate outcome of the deca-BDE assessment. From ACC's perspective, the revised RfD is improperly based on an unreliable study and is three orders of magnitude lower than it would be if based on the best available science. With a properly constructed process and panel, we would not be here today. Panel composition concerns could and should have been addressed prior to constituting the panel. Concerns with the science being relied upon could have been included in the panel's charge before the panel was even assembled. Instead, EPA's actions undermined the confidence that anyone, including the Agency itself, can have in either the process it followed or the resulting RfD.

ACC was pleased when EPA announced in 2003 that it would revise the IRIS file for deca-BDE. The existing RfD – the estimated amount of a substance that can be ingested daily for a lifetime without an appreciable risk of deleterious effects[1] -- dated from the late 1980s and was based on a study from 1975 on a commercial product that was significantly different from the product in commerce today. In the meantime, the National Toxicology Program – the federal government's flagship project for conducting animal testing to protect human health – had completed a pair of comprehensive, top-quality studies of deca-BDE exposure in rats and mice. In turn, the National Academy of Sciences' National Research Council – the federal gold standard for scientific peer collaboration in this area – had derived a human RfD using the two NTP studies. Finally, a well-conducted study from 2002 had evaluated the potential for deca-BDE to affect fetal development (and had discerned no ill effects). It seemed obvious that EPA would base the new RfD on this high-quality dataset.

Thus, ACC was surprised and alarmed to discover in December 2006 that EPA's draft toxicological assessment for deca-BDE (the technical support document underlying the IRIS file for a chemical) proposed to base the RfD on a highly questionable study from Sweden (the "Viberg" study). ACC was equally distressed to learn in February 2007 that EPA (through a contractor) had already convened an external panel to peer review the toxicological assessment. Finally, and exacerbating our concerns with the credibility of the panel and its processes, ACC was dismayed to read around the same time of statements made by the chair of the panel, statements that reasonably led it to conclude that the chair had made up her mind regarding deca-BDE before the panel had even met or concluded its evaluation.

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[1] http://www.epa.gov/ncea/iris/help_ques.htm#rfd.

The Viberg Study's Inadequacies

The Viberg study purported to demonstrate that a single dose of deca-BDE administered to young mice caused a neurological deficit, "disruption of habituation," as determined by a measuring device called a "Rat-O-Matic." Reliance on this study was highly inappropriate for a host of reasons:

- The study did not follow EPA "Good Laboratory Practices," or their European Union ("EU") equivalent, as any study would have to do if was being submitted to EPA by industry under the Toxic Substances Control Act ("TSCA") or the federal pesticide statute ("FIFRA"). "GLPs" provide quality assurance for laboratory data and allow full auditing of laboratory analysis to help ensure its scientific integrity.
- The study did not follow EPA's study protocols for developmental neurotoxicity testing, again as would be required for any study being submitted to EPA under TSCA or FIFRA. Indeed, in its review of the study for purposes of EPA's Voluntary Children's Chemical Evaluation Program, the Agency's Office of

Pollution Prevention & Toxics (OPPT) has stated that Viberg did not follow accepted methodologies for assessing neurological effects.[2]

- The methodology that Viberg did follow had numerous shortcomings. Most notably, OPPT determined that the study had a "fundamental flaw": it treated pups from the same litter as independent from each other, when a proper developmental study regards the litter as the basic analytical unit, because siblings tend to be similar to each other.[3]
- Perhaps most troubling, the study's author repeatedly refused requests from EPA, EU and industry officials for additional data that might answer their many questions about the study. A failure to supply sufficient data to allow others to reproduce a study renders the study unreproducible, and hence not "objective" within the meaning of Office of Management and Budget's (OMB)[4] and EPA's Information Quality Guidelines.[5] Both of these guidelines recognize that transparency about data and methods is an indispensable element of influential scientific information such as an IRIS file. Such transparency is not just a concern of industry or government, moreover; NGO groups widely endorse a

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[2] EPA Voluntary Children's Chemical Evaluation Program (VCCEP), *Data Summary: Update from the Original VCCEP Submission Dated Dec. 17, 2002 and the Peer Consultation Meeting in April 2003 – Decabromodiphenyl Ether* (Feb. 29, 2008), p. 47, available at http://www.epa.gov/oppt/vccep/pubs/sum22908.pdf.

[3] *Id.* at 42.

[4] OMB, *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies*, 67 Fed. Reg. 8460 (Feb. 22, 2002).

[5] EPA, *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency*, EPA/260R-02-008 (Oct. 2002), pp. 20-21, available at http://www.epa.gov/quality/informationguidelines/documents/EPA_InfoQualityGuidelines.pdf.

> requirement that, in order for a study to be relied upon by EPA, the study's author must supply underlying data upon request.[6]

Both EPA and EU regulators have concluded that the Viberg study was not adequate for use in supporting quantitative risk assessment; such as setting health effects values like an RfD.[7] More bluntly, EPA's Voluntary Childrens Chemical Evaluation Program (VCCEP) concluded just this February that "Viberg et al.'s results do not provide substantive evidence of a developmental neurotoxic effect due to decabromodiphenyl ether."[8] Remarkably, the very EPA scientists who considered the peer review report for purposes of conducting the IRIS review of deca-BDE state on their website that they have "low" confidence in the Viberg study.[9]

Failures in EPA's Peer Review of Deca-BDE

A key reason that the IRIS file for deca-BDE is substantively flawed is the process by which its underlying assessment was peer reviewed. As discussed below, serious failures of transparency and integrity render the entire process unreliable.

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[6] *See, e.g.*, Center for Progressive Reform, *Saving Science from Politics* (July 2008), p. 7, available at http://www.progressivereform.org/articles/SavingScience805.pdf.

[7] EPA, *VCCEP Data Needs Decision Document of Decabromodiphenyl Ether* (June 2005), p. 15, available at http://www.epa.gov/oppt/vccep/pubs/finaldeca.pdf.

[8] VCCEP Data Summary, supra note 2, at 47. The IRIS database began as an EPA consensus process, but in the case of deca-BDE, it is clear that the IRIS file does not reflect such a consensus.

[9] http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=0035.

Scientific peer reviews at EPA are governed by EPA's *Peer Review Handbook.*[10] This publication – which is widely endorsed across the spectrum, from ACC to environmental NGOs – cogently describes a deliberative process for conducting agency peer reviews of scientific and technical studies. If the process for the peer review of the deca-BDE toxicological assessment had followed recommendations of the *Handbook*, very likely the problems described above and below would not have occurred. Unfortunately, the deca-BDE peer review failed to follow several key recommendations of the *Handbook*:

- The public was not notified before the peer review panel was formed, and thus was unable to nominate proposed reviewers. The *Handbook* states that EPA staff managing peer reviews "should . . . consider requesting that the public, including scientific and professional societies, nominate peer reviewers.[11] It also notes that EPA's Science Advisory Board (SAB) routinely solicits such nominations to make sure that it gets the best possible reviewers.[12]
- The public was not provided with a list of proposed reviewers upon which it could have commented. Again, the *Handbook* notes that the SAB solicits nominations on a draft slate of reviewers so that interested persons can express support for or concerns about them.[13]
- The peer review panel was chaired by an individual who had not been adequately vetted, and who in fact had made public statements declaring her commitment to banning deca-BDE without waiting for any more scientific results. This major failing is discussed below.

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[10] EPA Science Policy Council, PEER REVIEW HANDBOOK (3d ed. May 2006).
[11] *Id.* at 60.
[12] *Id.* at 61.
[13] *Id.*

EPA's Process for Evaluating Potential Peer Reviewers

The *Handbook* is clear that "[t]he choice of peer reviewers should be based primarily upon the reviewers' expertise, knowledge, skills, and experience . . . . The group of reviewers should be sufficiently broad and diverse to fairly represent a balanced range of technically legitimate points of view."[14] The Handbook frankly recognizes that "experts with a stake in the outcome – and therefore a conflict or appearance issue – may be some of the most knowledgeable and up-to-date experts because they have concrete reasons to maintain their expertise."[15] On the other hand, federal statutes prevent EPA from using as peer reviewers either (i) individuals with current financial conflicts of interest or (ii) individuals who appear to lack impartiality.[16] The Handbook admits that decisions regarding impartiality are "not . . . clear cut" and "a judgment" call, due to the fact just noted that knowledgeable experts generally have views regarding the issues on which they are expert.[17] However, it states that, "[a]s a general rule, experts . . . *who have clearly 'taken sides,'* may have an appearance of a lack of partiality . . . and should be avoided."[18] The National Academies and NGO groups draw a similar line.[19]

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[14] *Id.* at 60.

[15] *Id.* at 70.

[16] When EPA conducts the peer review itself, the bar arises from rules implementing the Ethics in Government Act, 5 C.F.R. Part 2635, Subparts D & E; when EPA uses a contractor, as in the case of deca-BDE, the bar arises from the federal acquisition regulations, 48 C.F.R. § 9.505 (Federal Acquisition Regulations) & Subpart 1509.5 (EPA Acquisition Regulations); *see generally* EPA's *Peer Review Handbook* at 63-68. EPA can waive conflicts or partiality if they are outweighed by the need for the person's expertise.

[17] *Handbook* at 64.

[18] *Id.* at 63.

Public statements made by the person appointed to chair the deca-BDE peer review panel could reasonably lead to the perception that she had clearly taken sides and was unwilling to consider other perspectives. The chair:

- Was reported as saying "there is no question in [my] mind that deca-BDE should be eliminated because it is a persistent toxin that accumulates in the food chain."[20]
- Testified before the Maine legislature in support of a report specifically advocating that the state mandate a phase-out of deca-BDE.[21]
- Was quoted as saying she would support use of an equally toxic alternative to deca-BDE because "[t]he reason we are in this bind is because the industry doesn't

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[19] The National Academies state: "Potential sources of bias are not necessarily disqualifying for purposes of committee service. Indeed, it is often necessary, in order to ensure that a committee is fully competent, to appoint members in such a way as to represent a balance of potentially biasing backgrounds or professional or organizational perspectives. For example, an individual may be selected to serve on a committee conducting a broad study of proposed new scientific missions in space, although the individual is a consultant or an employee of an aerospace company that has a general business interest in such matters. . . . Some potential sources of bias, however, may be so substantial that they preclude committee service (e.g., where one is totally committed to a particular point of view and unwilling, or reasonably perceived to be unwilling, to consider other perspectives or relevant evidence to the contrary)." *National Academies' Policy on Committee Composition and Balance and Conflicts of Interest* (May 12, 2003), available at http://www.nationalacademies.org/coi/bi-coi_form-0.pdf. NGO groups agree: "As the [National Academies'] guidelines recognize, some degree of bias is unavoidable. . . . On the other hand, when biases become so strong that they impinge on an individual's ability to objectively answer new questions, that person should not be given the institutional power of an advisory committee member." *Saving Science from Politics, supra* note 6, at 27.

[20] *DEP Urges Legislative Ban on Fire Retardant*, BANGOR DAILY NEWS, Feb. 16, 2007, at B4.

[21] *Brominated Flame Retardants, Third Annual Report to the Maine Legislature* (Jan. 2007), available at http://maine.gov/dep/rwm/publications/legislativereports/pdf/finalrptjan07.pdf.

> have to collect any data about the compounds they are putting into commerce."[22]

This bias was confirmed by a later discovery: the chair was quoted in the SEATTLE POST INTELLIGENCER as saying "[w]e know enough now to ban deca. . . . because of bioaccumulation, because of the persistence, and I think we have enough hints of its toxicity. We don't need to wait another five years or even another two years and let an increase in the environment, while we nail down every possible question we have."[23]

ACC wrote and met with EPA to express its concerns when ACC learned about the chair selected for the toxicological assessment of deca-BPE. At this late date (the panel submitted its final report to EPA in April 2007), there really was no satisfactory way to undo the damage caused by the flawed process, including the chair's leadership role in the panel. Convening an entirely new panel was the best action EPA could take, but ACC doubted that such a request would be considered seriously. As a result, ACC was reduced to stating that, in light of the "policy predisposition" revealed by the chair's actions and statements, "ACC believes that the Agency must base its final Toxicological Review on data, opinions, and conclusions other than the Chairperson's. Otherwise, the integrity of this peer review will be further compromised – which ultimately calls into question the overall integrity of the entire IRIS database."[24]

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[22] *Id.* The statement is incorrect, by the way. The kinds of information that TSCA requires industry to provide, or authorize EPA to require, are summarized in EPA, OVERVIEW: OFFICE OF POLLUTION PREVENTION & TOXICS PROGRAMS (April 2007) at 3-20, available at http://www.epa.gov/oppt/pubs/oppt101-042007.pdf.

[23] *PBDEs: They are everywhere, they accumulate and they spread*, SEATTLE POST INTELLIGENCER, March 28, 2007, available at http://seattlepi.nwsource.com/local/309169_pbde28.html.

Notably, ACC advised EPA of this information and the positions the chair previously had taken. ACC did not call for Dr. Rice to be ousted as chair and did not "argue that scientific expertise with regard to a particular chemical and its human health effects is a basis for disqualification from a peer review board."[25] To the contrary, the chair's academic credentials are not in dispute and we appreciate her public service. Furthermore, ACC agrees with the *Peer Review Handbook* that "[t]he choice of peer reviewers should be based primarily upon the reviewers' expertise . . . ."[26] But it also agrees with the Handbook's statements about lack of impartiality. ACC also notes that NGOs have asked EPA to strike knowledgeable industry reviewers from peer review panels for the very same concerns about partiality.[27]

NGOs also weighed in, expressing concern in March regarding another member of the deca-BDE peer review panel. The letter from NRDC and six other NGOs objected to the service of Richard Bull on the grounds that he had previously been asked to resign from a

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[24] Letter from Sharon H. Kneiss, ACC to George M. Gray, EPA (May 3, 2007), at 6.

[25] Letter from Chairmen Dingell and Stupak to EPA Administrator Johnson (March 13, 2008), at 1.

[26] *See* note 14 *supra*.

[27] The March 13 letter sent in this investigation by Chairmen Dingell and Stupak to EPA Administrator Johnson was derived in part from a June 2006 letter from NRDC, EWG, CSPI and 22 other NGOs to EPA that sought to keep nine industry scientists off an SAB panel on ethylene oxide. The NGOs objected to three individuals because they "have *publicly taken a position* on the quantitative cancer risk of [ethylene oxide]." They concluded: "Committees whose members have . . . *a strong bias* . . . undermine the credibility of the EPA."

National Academies committee for failing to disclose, during the pendency of the committee, that he had been a paid consultant to a company in litigation over the same chemical that the committee was assessing.[28] This letter raises further question about the process by which EPA assembled and conducted the deca-BDE peer review.

EPA ultimately deleted the chair's statements from the peer review panel's final report. But the damage was done – as just noted, the panel had completed its work, and EPA's IRIS staff had already reviewed the reviewers' draft report. EPA's action therefore was about as ineffective as a judge instructing a jury to disregard something they had just heard a witness say. The final toxicological report conformed to the chair's recommendations; most important, it continued to rely on the unreliable Viberg study. Symbolically, while the chair's name may have been removed from the final report of the peer reviewers, she remains listed today as chair of the panel in the final toxicological assessment.[29] And disturbingly, when EPA initially removed the chair's comments from the final document, it failed to note that the final report had been revised or the reasons for that revision. ACC wrote the Agency a letter suggesting that it explain why the peer review report had been changed.

EPA issued its revised RfD for deca-BDE on June 30 of this year. The IRIS file relies on the Viberg study, and cites the flawed peer review report as support for doing so. It gives short shrift to or ignores ACC's substantive criticisms of the Viberg study and its procedural criticisms of the peer review process. Thus, it should be clear that EPA's attempts to "un-ring the bell" of the chair's biased stewardship of the peer review panel, whether or not sincere, had no effect on the ultimate result. Instead, EPA has posted a new IRIS file for deca-BDE which declares that EPA has "low" confidence in both the Viberg study upon which it has just relied and the RfD that it has derived from that study.[30]

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[28] Letter from Richard Wiles et al. to Stephen Johnson and George Gray (March 17, 2008), available at http://docs.nrdc.org/health/hea_08031701A.pdf.
[29] *See* page xi of the toxicological assessment, available at http://www.epa.gov/ncea/iris/toxreviews/0035-tr.pdf#page=84.

Conclusion

ACC thanks the Subcommittee for initiating this inquiry. By shedding light on the numerous process failures involved in EPA's recent reassessment of deca-BDE, this hearing could be the beginning of an effort to ensure that EPA follows its own Peer Review Handbook and related process guidance more closely. Until it does so, the integrity of peer review at EPA and the integrity of the IRIS database will both be at risk, because if you don't have confidence in a process, you can't have confidence in its result. Ultimately, it is the public that will suffer the greatest loss.

Once again, I appreciate the opportunity to provide this statement to the Subcommittee, and I would be happy to answer any questions that the Subcommittee has.

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[30] *See* note 9 *supra.*

Summary

The integrity of EPA's review processes are critical to the integrity of EPA's scientific databases. Fundamentally if you don't have confidence in the process, you can't have confidence in the result. In this case, EPA's stated procedures for peer reviews – on paper – are appropriate. In particular, EPA's *Peer Review Handbook* is a clearly written summary of the principles and procedures that should govern an agency peer review. It lays out the criteria for selection of peer reviewers, and it also describes the process for making those selections.

This June, EPA concluded the process of revising the oral reference dose or "RfD" for decabromodiphenyl ether (deca-BDE), a crucial flame-retardant. The many ways in which EPA failed to follow its own processes for scientific standard-setting, have resulted in an RfD in which EPA itself says it has "low confidence." The process was seriously flawed and the credibility of the outcome was its victim.

The story of the deca reassessment is a litany of processes that were not followed, and the consequences of those failures for the integrity and transparency of EPA's scientific enterprise and the public that relies on it. This flawed process resulted in two major failures. First, EPA used a completely inappropriate study to set the RfD. Second, the chair of the external peer review supporting the assessment had made numerous public statements indicating that she had made up her mind on the science and would not be willing to entertain evidence or opinions to the contrary.

The hearing presents a timely and important opportunity to highlight and investigate these failings in EPA's processes and their potential consequences for the integrity of science at EPA.

Mr. STUPAK. Well, thank you for your testimony. We will start with questions.

Ms. Kneiss, as I read your testimony, I get the impression that ACC thinks that the deca peer review process was flawed not just because of Dr. Rice's participation but also because you didn't have a say in the selection of the peer reviewers, and I think in your opinion, the peer reviewers relied on a scientific study you don't agree with. Is that correct?

Ms. KNEISS. Our concern was with the lack of following the process that EPA has in their handbook to follow on how to form a peer review panel.

Mr. STUPAK. But they don't need your input to do a peer review panel.

Ms. KNEISS. The guidelines do state that they should consider putting together a panel and they start by——

Mr. STUPAK. Right, but they don't——

Ms. KNEISS [continuing]. Alerting the public that they are going to do a peer review and seeking input on those panels and——

Mr. STUPAK. So you wanted input on the panel, who was going to be on the panel?

Ms. KNEISS. We would like them to follow the handbook as they have——

Mr. STUPAK. That is not what I asked you. ACC wanted input on who was going to be on the panel?

Ms. KNEISS. We wanted input on an open and transparent process, open to the public.

Mr. STUPAK. Well, if you have input, then how can the panel be said it is not biased then, if you put your people on it? Don't they come with preconceived ideas then or biases, as you said?

Ms. KNEISS. The key with a peer review panel is that it is broadly constructed, first of all, that I have the——

Mr. STUPAK. Sure. There are five people on this panel, right?

Ms. KNEISS. Correct.

Mr. STUPAK. OK. So they represent different views, right?

Ms. KNEISS. I would assume so.

Mr. STUPAK. OK. And some of them might agree with your view and others might not, right?

Ms. KNEISS. That is possible.

Mr. STUPAK. And a peer review panel analyzes everything including that Viberg report that you mentioned. They can take that into consideration. They can take all kinds of information and they make an assessment and give it to the EPA, right?

Ms. KNEISS. Correct.

Mr. STUPAK. And then there is time for public comment, correct?

Ms. KNEISS. Yes.

Mr. STUPAK. So why would you have Dr. Rice, why would you want Dr. Rice removed then?

Ms. KNEISS. It goes to the open process, the transparency of the process, the need to form a panel——

Mr. STUPAK. What was not transparent in this process?

Ms. KNEISS. We had no idea who was on the panel until the panel actually met and deliberated. We had no opportunity——

Mr. STUPAK. Then why didn't you ask all five people on the panel be removed then? Why just Dr. Rice?

Ms. KNEISS. Because the process was so flawed and it was so late in the process, we felt that our opportunities, quite frankly, were limited on how we could rectify the many problems with the process.

Mr. STUPAK. So why do you pick on one of the peer reviewers, why not all five of them then?

Ms. KNEISS. There were clear indications in the media and I might note that the EPA handbook clearly says that while you need knowledgeable experts as a general rule, those who have taken sides should not be put on the peer review panel because there is——

Mr. STUPAK. Were these statements of Dr. Rice before or after she was on the panel?

Ms. KNEISS. It is both.

Mr. STUPAK. Both? OK. Well, on page 4 of your testimony you state that deca was subject to an extensive 10-year study by the European Union as well as other major studies and has been found to present no significant risk to human health or the environment. Is that correct?

Ms. KNEISS. That is correct.

Mr. STUPAK. Didn't EU ban deca in 2002?

Ms. KNEISS. No, not deca.

Mr. STUPAK. They didn't?

Ms. KNEISS. It was other brominated flame retardants.

Mr. STUPAK. OK. Did they just ban it this year, deca?

Ms. KNEISS. No, it is still in use—oh, excuse me. I am sorry. I am confused. But they do have a risk assessment that had found that it is safe for use.

Mr. STUPAK. That is safe for use?

Ms. KNEISS. Yes. There is a risk assessment that took 10 years to complete and looked at 580 studies.

Mr. STUPAK. OK. Has deca been banned in Maine and Washington?

Ms. KNEISS. That is my understanding.

Mr. STUPAK. OK. On page 8 of your testimony, you state very strongly that transparency about data and methods is an indispensable element of influential scientific information such as the IRIS file, correct?

Ms. KNEISS. That is correct.

Mr. STUPAK. So I gather you would agree with the GAO, who testified earlier, and I noticed you were in the room at the time, that comments made on IRIS assessment by OMB and other federal agencies should be part of the public record. Do you agree with that?

Ms. KNEISS. We have supported improvements in the IRIS process for many years, improvements that would——

Mr. STUPAK. So you would agree with the GAO testimony earlier today then?

Ms. KNEISS. We agree with many of the recommendations from GAO that——

Mr. STUPAK. No, I am asking about their testimony today about the IRIS and transparency. Would you agree or disagree?

Ms. KNEISS. We agree with IRIS and the need for transparency.

Mr. STUPAK. OK. You allege that Dr. Rice—this is on page 12 now—testified before the Maine Legislature in support of a report specifically advocating that the State mandate a phase-out of deca BDE. Isn't it true that what Dr. Rice really testified on was the issue of whether there were safer chemicals available as substitutes? Isn't that what she testified?

Ms. KNEISS. My understanding is one of the statements was that there should be a phase-out of deca BDE.

Mr. STUPAK. Do you have a copy of her——

Ms. KNEISS. She did address other——

Mr. STUPAK. Do you have a copy of her testimony or anything where you could point to that?

Ms. KNEISS. I do have it, but not with me. We can get it to you.

Mr. STUPAK. Isn't it true that she did not testify before the Maine Legislature to recommend the phase-out of deca? She never recommended a phase-out of deca to Maine, did she?

Ms. KNEISS. She supported a report that recommended a phase-out.

Mr. STUPAK. Right, but my question was, she never testified before the Maine Legislature the phase-out, did she?

Ms. KNEISS. Part of her testimony was the support of a report that recommended a phase-out.

Mr. STUPAK. Do you have that report?

Ms. KNEISS. Yes, we will submit it to the Committee.

Mr. STUPAK. So let me ask you this. The role of the peer review panel is to receive an array of opinions on the safety of the chemical in question, and this one is deca, right?

Ms. KNEISS. Correct.

Mr. STUPAK. And isn't it the opinion of your organization, ACC, that only likeminded individuals should be on that panel then?

Ms. KNEISS. Oh, absolutely not. We believe that it is important to the credibility of the process that it be broadly constructed, that it reflect all of the technically legitimate beliefs.

Mr. STUPAK. Well, on this review panel, there are five people. Did they all submit their comments to the EPA on this deca?

Ms. KNEISS. As part of the process?

Mr. STUPAK. Yes.

Ms. KNEISS. Yes.

Mr. STUPAK. And did they all reach the same conclusion as Dr. Rice, all five of them?

Ms. KNEISS. I can't speak directly to—they all commented on different aspects.

Mr. STUPAK. And they all basically came to the same conclusion, did they not?

Ms. KNEISS. On certain aspects.

Mr. STUPAK. So they all agreed?

Ms. KNEISS. I guess so.

Mr. STUPAK. So if you are concerned about the makeup of this panel and Dr. Rice, it sounds like the other four people agreed with Dr. Rice, correct?

Ms. KNEISS. We have concerns that go far beyond Dr. Rice. It goes to the process and how the process was conducted and the failed process that resulted in the result that it did. It had many failings.

Mr. STUPAK. But these other four people gave the same conclusion as Dr. Rice so they are all wrong?

Ms. KNEISS. What we were saying was, the appropriate response would have been to reconstruct the entire panel to make sure that it reflected the broad range of views and we didn't have that.

Mr. STUPAK. Why didn't you object to the other four? Because they did exactly what you wanted. They got Dr. Rice off and the other four agreed with Dr. Rice so the report should really be that we should ban deca.

Ms. KNEISS. This was a process in our view that was conducted in the early stages in secret. We had no idea who the peer reviewers were. We had no idea what their credentials were or what their potential conflicts of interest were. By the time we found out, we were so far into the process, we felt that our options were very limited.

Mr. STUPAK. Dr. Rice, let me ask you this. What were you asked to do in this panel? What were you tasked to do, this peer review panel on deca?

Ms. RICE. A peer review panel, the chair of a peer review panel, really, their only obligation or their obligation is to hear all of the scientific opinions. We are presented with a series of charge questions by the Environmental Protection Agency. We can address other questions as well if we want to. But what I did in the peer review meeting was, I basically went around the table for each charge question and made sure that the opinions of all of the scientists, all four of the other scientists as well as myself, were heard and I think it is important to understand that these peer review panels, unlike some other panels that EPA convenes, there is no requirement for consensus. We don't have to reach a conclusion. We really submit our individual comments to EPA and then EPA responds to those.

Mr. STUPAK. And when all five people entered their comments to the EPA, were they similar to your comments?

Ms. RICE. I think that all of the comments for the most part were very similar. The bottom line, the whole purpose of this is to derive a so-called safe level, and the comments of all of us really came down in just ultimately just about the same place, so my comments were not outliers.

Mr. STUPAK. And one of the panel members had ties to industry?

Ms. RICE. Yes.

Mr. STUPAK. And they reached the same conclusion you did?

Ms. RICE. Yes. He was a perfectly reasonable scientific member of the panel.

Mr. STUPAK. Do you know, did ACC ask for the removal of any other member other than yourself?

Ms. RICE. To my knowledge, no, not from the correspondence I have seen.

Mr. STUPAK. OK. My time is up. We will come back for a second round. I will go to Mr. Shimkus for questions right now.

Mr. SHIMKUS. Thank you, Mr. Chairman. Because Greg Walden was so gracious in helping me out, I am going to defer and let him take it.

Mr. WALDEN. All right. Thank you. Thank you, Mr. Chairman, and thank you to our ranking member.

Ms. Kneiss, I want to go back to what you were saying. It sounds to me like the EPA didn't follow its own guidelines. That is your argument?

Ms. KNEISS. That is correct.

Mr. WALDEN. And the part of the guidelines they didn't follow was how you impanel and make sure the public whether you are for or against, in between has a right under their own guidelines to understand that a panel is going to be created and to have some ability to have input into how that panel is structured.

Ms. KNEISS. Correct.

Mr. WALDEN. Or who is on it. Is that right?

Ms. KNEISS. Correct.

Mr. WALDEN. And so our friend Dr. Sass at NRDC, has your organization ever weighed in on the creation of a panel? Has your organization ever weighed in on any particular panel member?

Ms. SASS. I have been there 8 years, and one of my primary tasks is to look at these kinds of issues, and I have never commented on a peer reviewer. I have never contested a peer reviewer and I didn't contest any of the peer reviewers on this panel.

Mr. WALDEN. So your testimony is, NRDC has never done that in any case?

Ms. SASS. Not on a peer review panel.

Mr. WALDEN. Not on Dr. Bull?

Ms. SASS. Not on a peer review panel. Dr. Bull, when I contested him, was on a National Academies panel, very different from this peer review panel. They draft the document in a single consensus report as the final outcome, and at that point I showed evidence that he was on the payroll to Lockheed Martin on an issue in litigation on a pollutant that Lockheed Martin would be responsible for.

Mr. WALDEN. And you wrote that to EPA?

Ms. SASS. It was not an EPA panel. It was National Academies and it was a panel that would write a consensus report on that chemical.

Mr. WALDEN. But did you raise that issue, that information with EPA at any time?

Ms. SASS. To try and contest Dr. Bull's——

Mr. WALDEN. No, did you present any information to EPA relative to Dr. Bull that concerns you on the deca panel?

Ms. SASS. The letter that I wrote said why should someone like Dr. Rice be removed from a panel when there are other people that have actual biases that weren't removed, but I never——

Mr. WALDEN. So you never specifically referenced Dr. Bull then in your correspondence?

Ms. SASS. In that letter I did but I never opposed his——

Mr. WALDEN. Could you provide that letter to us?

Ms. SASS. Sure. Also you might want to look at the peer review handbook guidelines, page 61, because it refers to the specific panel as actually put together by a contractor. But for the contract mechanism, the contractor may have its own pool of scientific and technical experts that it chooses from and EPA is actually not permitted to direct the prime contractor or the subcontractor in that process.

Mr. WALDEN. OK. So is there a process ahead of that though that EPA is supposed to follow in selecting the contractor or—so what you are reading overrides the other EPA guidelines? Is that what you are testifying to?

Ms. SASS. No. There is a real confusion about panels and committees here. But there is basically three different types. This committee was a peer review and there is not a consensus report that comes from it.

Mr. WALDEN. Correct. I understand.

Ms. SASS. And every opinion counts, so I agree that it is important to have a wide variety of opinions coming in as long as they are scientific criticisms. That is what EPA would want to collect. For a federal advisory committee, they have a single report and then for the National Academies also a single report and consensus. They write the report.

Mr. WALDEN. So what impact, Dr. Sass, did removing Dr. Rice's comments have on the substance of the peer review? Are you aware of, did it affect the substance in the end?

Ms. SASS. As much as I am aware, it didn't change the outcome very much at all. Essentially most of the peer reviewers had basic agreement. So there was really no reason to contest—I would not contest a peer reviewer at all.

Mr. WALDEN. I understand.

Ms. Kneiss, if I could go back to you, because the question has been raised, why did you pick on Dr. Rice. I mean, that is the substance of the question here, and what you have testified is, there were public comments attributed to her that indicated from your perspective that she had a bias going in.

Ms. KNEISS. That is correct.

Mr. WALDEN. Were there public comments attributed to other members on that peer review panel that showed bias either for or against——

Ms. KNEISS. We weren't aware of any.

Mr. WALDEN. Is she the only one then that you had public information on that indicated——

Ms. KNEISS. In terms of public comments, yes.

Mr. WALDEN. And is that why your organization——

Ms. KNEISS. That is correct. At that late point in the process, from our perspective and according to the guidelines, this should have all been resolved before the panel was put in place. There was not the opportunity to do that.

Mr. WALDEN. Now, what about this issue Dr. Sass just raised, that this was a different type of panel that was created under a contractor and therefore, I assume you are saying, not subject to that rule. Is that your understanding of it?

Ms. KNEISS. Our understanding is that the guidelines are still important to that process and there is a lot of requirements in there that suggest that it be open and it be an open and transparent process.

Mr. WALDEN. Personally, I think that is the way they all should be, regardless of the side of the issue you are on. I know we had a situation in my district where an organization that was on the GAO approved list to simply take data that had been accumulated and transcribe it. No scientific input whatsoever. And an environmental organization objected and there was quite a stir raised including a full investigator IG report done because the allegation was this group was biased because they also were certified to do consulting work with mining organizations. At the end of the day, the IG said it was all bogus, this group did what they were supposed to do, it was all legitimate but not before it was a page 1 story and all that. So there is a lot of give and take when it comes to areas of dispute and especially when it comes to this type of science because there are a lot of high emotions. If you have bad chemicals running around a school, you want to make sure your kids are safe. So I guess the question is, how do we fix this? How do we fix this? And Dr. Rice, does something need to be changed here? If there was somebody—let us say—sorry, I will let you answer. Let us say somebody had the opposite view you held or allegedly hold, which is that this is a wonderful chemical and there are no problems to it, should somebody be able to object to that person being on a peer review panel?

Ms. RICE. Yes, I think that people should be able to object before the fact. I agree with that. EPA personnel can also challenge the— I mean, when I was at EPA, EPA people could also challenge the choices of the contractors for conflict of interest or for lack of the appropriate expertise, which is the only two things that really should matter.

Mr. WALDEN. So you don't have an objection to—I mean, personally you might, I understand and respect that—either Dr. Sass or Ms. Kneiss being part of that public process to weigh in for or against somebody being on one of these panels but then it is ultimately up to the——

Ms. RICE. Ultimately it is up to the contractor to respond to that or not. That is the level at which it should have happened. After a panel is held to go back to EPA, which was the only thing that they could do at that point, is not——

Mr. WALDEN. Was there an opportunity to object to the contractor?

Ms. KNEISS. No.

Mr. WALDEN. So that was the issue here at the core?

Ms. KNEISS. We were not—we had no idea what this process was, what it looked like, what the panel looked like, until their first meeting.

Mr. WALDEN. Do you concur with that, Dr. Sass, in this case?

Ms. SASS. Yes, and I think that we agree too that transparency is really paramount, because even if there is not a real problem, if you don't have transparency, the perception of the problem could be the problem. So I agree that EPA needs to be left to do its work and I also agree that anybody should be able to comment or write letters and provide information if they think it is relevant and that EPA should weigh the scientific comments appropriately and as much transparency as you can put in that process means you don't have to have a problem later.

Ms. KNEISS. Again, if you don't have confidence in the process, you don't have confidence in the result.

Mr. WALDEN. And the irony is, even with this dispute, those who don't like this chemical, actually the report seems to back up their view over what your organization would like to see come out of this whole process, right?

Ms. KNEISS. That is the result of the report, correct.

Mr. WALDEN. Mr. Chairman, I will yield back to my colleague from Illinois the final 57 seconds on my clock.

Thank you all for your testimony today.

Mr. STUPAK. Mr. Shimkus for questions.

Mr. SHIMKUS. Thank you, Mr. Chairman.

Dr. Rice, first of all, for everyone here, I have calmed down a little bit. So that should be good news. But you worked for EPA from 1993 to 2003. In fact, you received a level I scientific and technological achievement award from EPA for the high quality of your research, and I wanted to put that into the record and just thank you for your service. I thought about the first panel, I thought this is scientists playing politics or politicians playing scientists. I was trying to figure out. But that is part of this basic debate of peer review, whether they have—can they be objective if they come to the panel with already preconceived statements. So I am learning a lot, so I appreciate the first panel and this one, and I apologize for not being here for opening statements.

Dr. Rice, we have already had some discussions about Richard Bull as a member of the peer advisory panel and we all know that. Dr. Sass has obviously raised the issue. In your experience with the panel, do you believe Mr. Bull was impartial when reviewing the literature?

Ms. RICE. Yes, I believe that all five of us were impartial.

Mr. SHIMKUS. Yes. I mean, that is just part of this whole debate on both sides. So do you think it is possible to have ties or an affiliation with an advocacy group or industry and still be able to objectively interpret the data?

Ms. RICE. It is possible, yes.

Mr. SHIMKUS. If so, how can the EPA determine when someone's ties would make them impartial? What should the test be and how could it be implemented before a peer review panel is selected?

Ms. RICE. Well, I think one litmus test is whether a person has financial ties. I think that would delete them from the panel right from the get-go. But then after that, I think it gets a little bit murkier and I think that you have to look to whether the particular person is speaking from the science and certainly reasonable people, reasonable scientists can disagree on the interpretation of the science and that is OK. I mean, that is the way it works. But if there is a perception that the person is going beyond the science to talk about policy and that that is coming from some special interest, financial or otherwise, then that should disqualify them from the panel.

Mr. SHIMKUS. But in Bull's case, he had a financial tie.

Ms. RICE. Excuse me?

Mr. SHIMKUS. Bull's case, or was this another case?

Ms. RICE. It was another case that you are thinking of, yes. For this panel, he did not. I don't think he was in conflict.

Mr. SHIMKUS. So when these scientists are all in this room, five of you, if someone, and you are going on the scientific data, you all are professionals so you could probably tell if someone is way off the deep end on their analysis?

Ms. RICE. I think so.

Mr. SHIMKUS. OK. You went to Maine and of course we have covered the testimony and you reported to the Maine Legislature. How do you characterize your testimony before the Maine Legislature? We have heard what was asked. How would you, give us in your own words.

Ms. RICE. Well, the Maine bill was very specific, and the question before me, the question before the legislature was, were there safer alternatives to deca, and so, to do my job as a toxicologist, I had to look at the properties of deca and then the properties of the alternatives, and I have to say that my main concern with regard to deca was not really the toxicity. I think we know less about the toxicity than I would like to know. My concern really was that it is persistent in the environment, that it bioaccumulates up the food chain. It is found in breast milk. Most of us are carrying body burdens of deca. It breaks down in our bodies, into the environment to some of the chemicals, some of the PBDEs that had already been banned by Maine. You know, so that was the framework. That was the context. And in fact, the ACC has a quote from me in a newspaper where I say that there are hints about the toxicity, and it is important to understand that the EPA peer review panel was about toxicity. It didn't include at all anything about persistence, bioaccumulation, breakdown, to other forms of these PBDEs which I am on record as saying that those were my main concerns, and when I testified from Maine, the real problem that I had was determining, trying to determine whether the alternatives were safer, and the reason for that was because we know less about the alternatives than we do about deca or many of the alternatives than we do about deca. The toxicity data in particular aren't there and I ended up going to the European industry and getting some toxicity data from them for some of these alternatives because, you know, as a person advising the legislature, I really didn't want it on my conscience that I said there are safer alternatives when it turned out that there weren't.

Mr. SHIMKUS. Why would the—again, we are laymen so you are kind of saying there are two separate issues here. Why would the ACC say they are not, they are linked?

Ms. RICE. I personally think it is a mischaracterization because—in my testimony I said that the peer review of the EPA document and my work for the State of Maine were really two entirely different things. I feel that I am perfectly capable of being very objective about following EPA guidelines on how to set a reference dose. In fact, I did that for the Agency. I had no preconceived ideas about what the reference dose should be at all and I don't even think about the final number. I mean, I never do. I just follow the process and whatever it ends up being is whatever it ends up being.

Mr. SHIMKUS. Thank you.

Ms. Kneiss, the ACC raised a concern. Why did you all concur that there is a connection? Do you know?

Ms. KNEISS. It all goes to the flawed process to begin with. We had no information about how this process was going to move along, who was on it, what the credentials for the panelists even were. We had to FOIA that to find out the credentials of the panelists. And so it was a process in which we had very little confidence to begin with because it wasn't open and transparent. And then we had concerns with how the Agency took on studies and looked at studies which didn't follow their own scientific guidelines.

Mr. SHIMKUS. Great.

Dr. Rice, do you think this qualified as, in essence, the public pronouncement issue that the EPA uses to say oh, maybe she shouldn't be on the board, your testimony as a public pronouncement?

Ms. RICE. No, I don't at all because I really think that they are different issues, and I am perfectly capable of being objective in following the process to set a reference dose.

Mr. SHIMKUS. And I really appreciate these testimonies and this hearing.

Dr. Rice, having worked in the EPA, say going back to the last panel, did you as a scientist ever feel that you were bullied or pushed into making a scientific judgment based upon the political hacks that were appointed at the EPA?

Ms. RICE. Well, I left in 2003, and that was just beginning to happen, and I didn't leave because of that. A lot of people have asked me that, and I didn't. That was not the reason I left. But I really personally didn't.

Mr. SHIMKUS. Thank you.

Mr. Chairman, I think I am done. Thank you.

Mr. STUPAK. Let me just clarify a couple things. Dr. Rice, when you worked with the Maine Legislature at the time when you were talking to the Maine Legislature about deca, your work had already been done on this peer review panel, correct?

Ms. RICE. I think they overlapped. I think—I have handouts that are dated in April. The peer review met in February. I think I had testified before that once but I am not—I have to say that I am not really clear on the timeline because to me, these were completely separate events that really had nothing to do with each other.

Mr. STUPAK. And you are the State toxicologist so it would be normal for you to talk to the legislature about chemicals and on legislation they are proposing, things like that?

Ms. RICE. Yes. Their committee meetings are called work groups and I think——

Mr. STUPAK. It was a work group?

Ms. RICE. It was a work group and they asked me questions for an hour, and I was charged as the toxicologist to do this for the legislature.

Mr. STUPAK. And when you were put on this peer review, they knew you were the toxicologist for the State of Maine?

Ms. RICE. Yes, certainly.

Mr. STUPAK. Let me ask you this, Ms. Kneiss. You are familiar with the Peer Review Handbook, 3rd edition?

Ms. KNEISS. Yes.

Mr. STUPAK. OK. These are only guidelines.

Ms. KNEISS. That is correct.

Mr. STUPAK. There is nothing in there that requires industry to be consulted or to be made known of who is on peer review panels.

Ms. KNEISS. But it does recommend it.

Mr. STUPAK. Recommendation. It is a guideline. They are not required to get your approval before they do a peer review panel, correct?

Ms. KNEISS. That is correct.

Mr. STUPAK. OK. You have talked an awful lot about transparency, and you were here at the last panel so the new IRIS process doesn't allow for much transparency when OMB is involved, correct?

Ms. KNEISS. Well, what we believe—we have been supporters of an improved IRIS process for many years.

Mr. STUPAK. So you don't think——

Ms. KNEISS. And we believe transparency is very important in that process.

Mr. STUPAK. So in the IRIS process, OMB should open up their deliberations and their reports from Department of Energy, Department of Defense so we have this transparency you want, correct?

Ms. KNEISS. I can tell you, we haven't taken—we haven't looked specifically at that aspect of it. I can tell you——

Mr. STUPAK. Right, but——

Ms. KNEISS. From the broader point of view, we——

Mr. STUPAK. I am asking you, from your passionate concern for transparency, shouldn't we have transparency then in IRIS, including OMB, DOD, and DOE?

Ms. KNEISS. We should have transparency in the process. I do not know the specific issues surrounding that to make a statement on that particular aspect.

Mr. STUPAK. OK. Dr. Rice, in our exhibits here, in our exhibit book right there if you want to look at it, Exhibit #10, there is a letter from the governor of Maine, Governor Baldacci, to the EPA protesting your removal from the panel. Did you have anything to do with the governor writing that letter? Did you ask the governor to write the letter?

Ms. RICE. No, I found out about it after the fact actually. I appreciated it but I found out about it after the fact.

Mr. SHIMKUS. And Mr. Chairman, he is a former colleague of ours and I think we all hold him in high regard. I know I do.

Mr. STUPAK. Dr. Sass, can you say a little bit more about the increased secrecy under the new process of IRIS that undermines the scientific method and the public's right to know? Could you say a little bit more about that? You seem pretty familiar with it.

Ms. SASS. Right. I will comment on it but also I think I can't refer the whole group but at least in my written testimony that is being submitted because it has a table on page 9 and 10 where I really struggled to clarify the old and the new because, as you know, the new is far more complicated. But in essence, there was always an opportunity for interagency review and of course, the agencies are allowed to call each other any time they want, so that hasn't changed and they always had that opportunity under the old process, and also of course these always go to OMB for review. That was always done. The difference is that at this point they have inserted a number of new opportunities. They have obligated the IRIS process to incorporate new opportunities for interagency and OMB review, both early but also a final one at the end, and that the public doesn't have an opportunity during those times to comment. So they haven't increased public transparency or participation at all but they have increased the interagencies.

Mr. STUPAK. So with OMB at the end there, the public doesn't really have any input until the final rule comes out then so they don't know what happened between OMB and the final decision?

Ms. SASS. Right, which is very concerning to us, but the new rules do obligate the IRIS staff to have to respond and resolve those OMB concerns and our concerns are that they may not all be scientific so that there is agencies like DOD and DOE that are not public health agencies and we are concerned that comments that are not scientific comments may derail or alter the process.

Mr. STUPAK. Since you are the scientist familiar with this, Mr. Parshley mentioned this journal Regulatory Toxicology and Pharmacology as not being very credible in the eyes of some people but having a bias towards industry. Your opinion on that? Is Mr. Parshley right in his testimony?

Ms. SASS. This is a journal that has a number of industry-affiliated people on its editorial board and associate editorial boards and it is shown, has a tendency, a pattern of publishing articles that are very friendly to the industry perspective and they are specifically targeting regulatory decisions or chemicals that are undergoing regulatory review.

Mr. STUPAK. Let me ask Mr. Parshley, if I may. You take the mic there, if you would. You talked about toxaphene, and how does toxaphene damage your health? Do you know?

Mr. PARSHLEY. I am a project manager, and my job is really to get that information from the experts, and so I avoid trying to be the expert but when people ask me those type of questions, in my community when they come to me and ask those questions, I very often refer to ATSDR's toxicological profile for toxaphene, and then depending on whether it is adults or children, they get more specific about the different threats.

Mr. STUPAK. Well, do you have some understanding of the health risks of toxaphene? I mean, you are concerned about it being next to an elementary school. Why are you concerned? What are the health effects you are concerned about?

Mr. PARSHLEY. I am familiar with the issue. You know, my concerns are more than just with the elementary school, but at the elementary school itself, toxaphene is shown to have some developmental delays and so the very early years in school are important for children. Children's immune systems are not as robust, are not fully developed.

Mr. STUPAK. OK. Well, let me ask this question. Why are you after the EPA to do more studies then, your Glynn Environmental Coalition there?

Mr. PARSHLEY. We are not asking for more studies actually.

Mr. STUPAK. What are you asking the EPA to do then?

Mr. PARSHLEY. A process for measuring toxaphene that was developed it was only used in our community that did not report all the chemicals present. The Office of Inspector General found, agreed with us, and it was appropriate, particularly—we are not just dealing with toxaphene. We are dealing with toxaphene manufacturing waste, and so, you know, the argument of what is and what isn't toxaphene has gotten very convoluted but what we want is very simple, test, report all the chemicals present. Then the toxicologists can look at it and tell what we need to protect our children and our families.

Mr. STUPAK. Well, what chemicals do you think aren't being reported?

Mr. PARSHLEY. The Office of Inspector General was very specific. The previous method looked at only one part of the chromatogram and eliminated everything else. Well, in that part that they eliminated, there was chemicals in the toxaphene mixture that have six and seven chlorines, it is a whole group, and that is what is mostly in our community and it is the stable form and what is going to hang around for a long time. And he said, gee, you know, you are not reporting the chemicals that are present in the most amounts in the community. So other—why we need the data, we need to know, can public works clean out the drainage ditch and not recontaminate the school? When the life of the school is gone, does our community have an encumbered piece of property? These are other questions in addition to, are our children safe.

Mr. STUPAK. So what you are basically saying, you don't believe the EPA has adequately tested for toxaphene or the breakdown chemicals that come from toxaphene in the landfill near the school and in your community. Is that what you are saying?

Mr. PARSHLEY. Yes, but if I could clarify, there has been technical toxaphene, weathered toxaphene, breakdown toxaphene, I will tell you the definition we use. We went to the Hercules patent and they said, well, this is what we patent-protected and that is what we call toxaphene. All these different definitions all fall in there. It is all toxaphene. What has happened is, the different amounts or ratios of the individual chemicals have changed but it is all still toxaphene, so that is a good clarification. Over time, the ratio of the different chemicals has changed, how much the different chemicals are there, but it is still there. But what we need for our community, not only for protection of our children, we have an estuary where 2 to 3 million pounds were released. We need to be looking at what disciplines are going to use this data, the actual resource managers, people that are going to be looking at fisheries, not only protecting people from contaminated fish but what is the effect on wildlife and the recovery of our natural resources.

Mr. STUPAK. Have you asked EPA to do these studies?

Mr. PARSHLEY. Well, a study is built off of good, sound data. We need to know what is there is the first step and that is what we are asking is why I came here today is, we have a very simple request: test and report all the chemicals that are there. There is no reason on this earth to test and not report the chemicals that are there.

Mr. STUPAK. Very good.

Questions?

Mr. SHIMKUS. Thank you, and I will be brief. First of all, I was thinking about these rules of guidelines and I was thinking about Pirates of the Caribbean, are they rules or are they guidelines. That is part of the legislative challenges we have, the pirate rule.

I was interested in this magazine, Regulatory Toxicology and Pharmacology Journal, which now, Dr. Rice, are they a credible magazine, would you feel?

Ms. RICE. I agree with Dr. Sass that they tend to be biased toward industry.

Mr. SHIMKUS. So in your letter to the editor in 2004, titled "Critical Effect of Perchlorate on Neonates in Iodine Uptake Inhibition," why did you send the letter?

Ms. RICE. Because perchlorate is something that industry as well as government and various states are very concerned with. It was an appropriate place to put it. It was an appropriate audience for it.

Mr. SHIMKUS. Did you place it elsewhere?

Ms. RICE. No.

Mr. SHIMKUS. So they are credible enough for you to write a letter to inform the scientific community of this issue?

Ms. RICE. Yes, I am not saying that nothing is published in the journal that isn't reasonable and I am not saying that everything in the journal is biased. I am saying that when you take the body of studies as a whole, there tends to be a bias toward the industry point of view. But it is not an industry publication.

Mr. SHIMKUS. Great. I appreciate it. I was just trying to clarify. And I am not going to go long into this. On the next panel we have George Gray, who is the EPA director now. Dr. Sass, you have laid some pretty serious charges against him, a former member of the faculty of Harvard Center for Risk Analysis. Instead of just going into the excitable debate, can you provide for us e-mail, documents, memos, or anything that substantiates some of these touch charges you have laid up against Dr. Gray?

Ms. SASS. I don't think I have made any charges that would require e-mails to substantiate. I think what I—you would have to tell me but I believe what we have said is about the Harvard Center for Risk Analysis is that it takes money and it gets support from a number of industries. I mean, I can give you documentation for that.

Mr. SHIMKUS. You specifically cite the IRIS review of perc in the example showing Dr. Gray's interference with the IRIS process.

Ms. SASS. That was reported by a reporter in the trade press and I can provide that for you.

Mr. SHIMKUS. That is what we are asking. Do you have anything other than the trade press?

Ms. SASS. You have to go case by case and I will tell you what I have as evidence and provide it for you.

Mr. SHIMKUS. OK. And I will end there. Thank you, Dr. Sass.

Mr. STUPAK. Well, let me thank this panel for their attendance here today. I am going to dismiss you. We have votes on the floor. Dr. Sass, Mr. Shimkus, all members have a right to follow-up questions in writing, and I would urge the ranking member to do that if he so wishes to get more detailed information and we may do the same thing, Ms. Kneiss. So I thank you all for being here. Thank you for your testimony. We are going to be in recess for the next half-hour. We have four votes on the floor, so we are in recess.

[Recess.]

Mr. STUPAK. The hearing will come back to order. Sorry about the delay. We had an extra vote you guys threw in there we didn't know about, so we had a couple extra ones there. Let us get our last panel here and hear from them. On our third panel, we have the Hon. Marcus Peacock, who is Deputy Administrator of the U.S. EPA, and Dr. George Gray, who is the Assistant Administrator for the Office of Research and Development at the U.S. Environmental Protection Agency. Gentlemen, as you know, it is the policy of this subcommittee to take all testimony under oath. Please be advised that you have the right under the rules of the House to be advised by counsel during your testimony. Do you wish to be represented by counsel, Mr. Peacock, Mr. Gray?

Mr. PEACOCK. No.

Mr. GRAY. No.

Mr. STUPAK. OK. Then I am going to ask you to please rise and raise your right hand to take the oath.

[Witnesses sworn.]

Mr. STUPAK. Let the record reflect our witnesses replied in the affirmative. They are under oath. We will start with opening statements for 5 minutes. Your full statement will be part of the record. Mr. Peacock, should we start with you, sir?

Mr. PEACOCK. I don't have an opening statement, Chairman. I am here to answer any questions you may have.

Mr. STUPAK. Dr. Gray?

STATEMENT OF GEORGE M. GRAY, PH.D., ASSISTANT ADMINISTRATOR, OFFICE OF RESEARCH AND DEVELOPMENT, U.S. ENVIRONMENTAL PROTECTION AGENCY

Mr. GRAY. Well, thank you. Good afternoon, Chairman Stupak, members of the committee. I am George Gray, the Assistant Administrator for the Office of Research and Development at the Environmental Protection Agency. Thank you for the opportunity to appear before the subcommittee to discuss two important things: first, our ongoing efforts to maintain the highest levels of scientific integrity and research assessment and analyses at the U.S. EPA and our recent improvements to the Integrated Risk Information System, or IRIS.

First, research that is conducted by our scientists and grantees provides the scientific and technical information that we need to protect human health and the environment. During the past several years, EPA has taken a number of steps to maintain a program of sound scientific research to inform agency decisions without allowing regulatory objectives to guide or distort scientific findings or analyses. These steps include open, transparent, and peer-reviewed research planning and competitively awarded extramural research grants. It includes independent peer review of our science studies, publications, and assessments and rigorous independent evaluations of EPA's research laboratories and centers.

Science informs and provides a foundation for EPA's regulatory decisions. At the same time, it is very important to recognize that many scientific questions or assessments generally involve both science and science policy considerations. Similar to other federal agencies that are required to produce scientific assessments and also make regulatory decisions, EPA views the relationship between science, science policy, and decisionmaking as a continuum. To start, science is conducted by individuals or teams working in our laboratories, out in the field, or in academic institutions across the country. Their work is reviewed by subject matter experts in accordance with EPA's highly regarded peer review process and our information quality guidelines. Our scientists are encouraged to publish and otherwise communicate their findings. Our scientists and grantees published over 1,000 EPA scientific studies last year.

But by their very nature, scientific studies involve varying degrees of uncertainty so there is rarely a single best study or a single best answer that we can use in decisionmaking. Therefore, we rely on science policy and we need to synthesize and assess and make choices when we have a wide range of scientific opinions and data points. The science policy process may involve: filling in knowledge gaps with default assumptions; using weight of evidence approaches to make scientific inferences; or making specific choices. Science policy work draws on expert insight from multiple scientific disciplines and is further strengthened by agency, interagency, and public review.

In the mid-1980s, EPA program offices sometimes published very different toxicity values for the same chemical in spite of having access to the same scientific data. The original data was the product of science whereas the Agency toxicity values were a product of science policy as they included inferences, assumptions, and choices. EPA developed IRIS, the Integrated Risk Information System, exactly to help standardize the science policy process that is inherent in risk assessment. IRIS was originally intended to be an internal EPA system that provided EPA risk assessors and managers with an agency position on the potential human health risks of toxic substances. But to meet the growing public demand, the IRIS process has evolved over time. Examples of components that have changed include the setting of the annual IRIS agenda, levels of external peer review, and opportunities for public and interagency review.

In 2005, EPA initiated a formal process to document the steps in the IRIS process including formalizing recent improvements. On April 10, 2008, EPA announced the revised IRIS process, the first time that EPA has documented the entire process and made it available to the public. Prior to the release, the IRIS process had often been viewed as a black box, both within and outside of the Agency. It was unclear what steps compromised the process and what the timing was for each step or where opportunities existed for internal and external involvement. Our improvements in the IRIS process helped define the appropriate roles for public, agency and interagency comments and they also helped promote greater communication and sharing of information between all interested parties and EPA. This revised IRIS process is designed to provide greater transparency, objectivity, rigor, and predictability in IRIS assessments.

So in conclusion, EPA has a proud history of producing science that has informed decisions to help protect human health and the environment. We are committed to using the best available science and constantly evaluating our science policy choices to achieve our strategic goals and fulfill our mission. From the lab bench to the administrator's desk, we follow a science-to-decisionmaking continuum that is in common with other federal agencies that rely on both science and science policy considerations in their decision making.

So thank you, Chairman Stupak and members of this committee for this opportunity to describe EPA's critical scientific work, and I look forward to answering any questions you may have.

[The prepared statement of Mr. Gray follows:]

TESTIMONY OF

GEORGE M. GRAY, Ph.D.
ASSISTANT ADMINISTRATOR FOR RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
U.S. HOUSE OF RESPRENTATIVES

September 18, 2008

Good morning, Chairman Stupak and Members of the Committee. My name is George Gray, and I am the Assistant Administrator for Research and Development at the U.S. Environmental Protection Agency (EPA, or Agency). I also serve as EPA's Science Advisor. Thank you for this opportunity to appear before the Subcommittee to discuss three important topics: First, our ongoing efforts to maintain the highest levels of scientific integrity in research, assessments, and analyses; second, EPA's recent improvements to the Integrated Risk Information System (IRIS); and third, the Agency's independent, external peer-review process.

Scientific Integrity

EPA conducts research that provides scientific and technical information to support our mission to protect public health and the environment. Our scientists conduct research independent of political influence, publish results in peer-reviewed journals, present findings at scientific and technical conferences, and speak openly with the public about their work.

We are committed to using the best-available science and the most defensible science-policy choices to achieve our strategic goals and fulfill our mission. Science informs, and provides a foundation for, EPA's regulatory decisions. At the same time, it is important to recognize that what often appear to be purely scientific questions or assessments generally involve both "science" and "science-policy" considerations. For example, developing risk values requires many decisions, choices, and assumptions that are generally guided by Agency science policy.

While it is important to integrate our scientists' research and development products with the Agency's regulatory needs, it is also vital that the research itself is independent, objective, transparent, and of the highest quality. During the past several years, EPA has taken a number of steps to maintain a program of sound scientific research to inform Agency decisions without allowing regulatory objectives to guide or distort scientific findings or analyses. These steps have included open, transparent, and peer-reviewed research planning; competitively awarded extramural research grants; independent and external peer review of our science publications, assessments, and documents; and rigorous evaluations of EPA's research laboratories and centers.

EPA's science program is at the leading edge in many areas of science and technology. With our focus on high-quality, relevant support for the Agency's activities and decisions, we are well-positioned to address the challenges of the 21st century. We constantly look for ways to build on our strengths so that EPA's decisions and actions continue to be informed by the best-available science and the most defensible science-policy choices.

EPA's Scientific Staff

According to Thomson Scientific's *Essential Science Indicators*, over 20 percent of our publications are "highly cited" and over 30 percent are published in "high-impact" journals.

Our scientists are also active participants in many scientific organizations, including the American Public Health Association, Association for Practical and Professional Ethics, Geological Society of America, American Geophysical Union, Ecological Society of America, Air and Waste Management Association, Society for Risk Analysis, International Society of Exposure Analysis, Society of Toxicology, and more. Many of our scientists hold leadership positions in, and have received prestigious awards from, major scientific organizations such as the Intergovernmental Forum on Chemical Safety, International Commission on Radiological Protection, and Society of Toxicology, as well as major research universities.

Considering the scientific and technical talent in our organization, and our experts' clear commitment to public service, it is my aspiration to have EPA be the premier environmental-science organization in the federal government. We have demonstrated positive momentum toward this goal with many achievements, such as:

- Award-winning tools and strategies to protect public health developed by our National Homeland Security Research Center;
- Cutting-edge models to test chemical effects and interactions developed by our National Center for Computational Toxicology;
- Ground-breaking reports on the effects of climate change to inform national and international dialogues developed by our Global Change Research Program; and
- Grants awarded to scientists across the nation to research environmental challenges and develop innovative solutions through our National Center for Environmental Research.

Science Planning and Science Management at EPA

EPA's first priority is "doing the right science." A number of sources, both internal and external to the Agency, provide information and guidance on how EPA can prioritize its research. EPA's Strategic Plan serves as the first organizing principle for EPA's research agenda. Next, EPA's Program and Regional Offices communicate their science needs based on their unique policy and regulatory responsibilities. EPA's Office of the Science Advisor also provides critical input. The Agency must incorporate into its research planning Congressional mandates, the priorities of the Administration and other agencies, as well as advice from external advisory committees. Other research stakeholders, including non-governmental organizations and industry, may voice their priorities. EPA management and directors of research take input from these various sources into account when setting the research agenda.

"Doing the science right" by promoting effective management and implementation of our research strategies is an equally important responsibility and serves to strengthen scientific integrity. It is vital that EPA strive for the highest quality and credibility in its activities and decision-making processes if the American public is to have confidence in our decisions. To this end, EPA scientists, managers, and union representatives jointly developed the EPA *Principles of Scientific Integrity* under the auspices of the National Partnership Council. To ensure that management and staff understood the importance of scientific integrity at all levels of the organization, the release of this document was followed with online training. The Principles include the following:

- Honesty - EPA employees are responsible and accountable in all aspects of their science.
- Accuracy - Employees represent their work, and the work of others, fairly and accurately.
- Recognition - The intellectual contributions of others are recognized and acknowledged.
- Freedom from conflicts - All science is conducted in an atmosphere free of conflicts of interest.
- Knowledge of statutory authorities - Know and understand the statutes and regulations that guide EPA's work.
- Responsibility - Breaches of these principles must be promptly reported when discovered.
- Open-mindedness - Differing views and opinions on scientific and technical matters are a welcome part of the scientific process.

EPA's Criteria for Transparency further support the Agency's scientific quality. The Criteria for Transparency were written to ensure that the public would understand all the steps, logic, key assumptions, limitations, and decisions in the assessment process, and also comprehend the supporting rationale that led to a particular decision or outcome. EPA's 2000 *Risk Characterization Handbook* states that transparency includes full disclosure of the following:

- The assessment approach employed;
- The use of assumptions and their impact on the assessment;
- The use of extrapolations and their impact on the assessment;
- The use of models *vs.* measurements and their impact on the assessment;
- Plausible alternatives and the choices made among those alternatives;
- The impacts of one choice *vs.* another on the assessment;
- Significant data gaps and their implications for the assessment;
- The scientific conclusions identified separately from default assumptions and policy calls;
- The major risk conclusions and the assessor's confidence and uncertainties in them; and
- The relative strength of each risk assessment component and its impact on the overall assessment.

To monitor performance, EPA'S Office of Research and Development (ORD) requests feedback from EPA Program and Regional Offices on the timeliness and quality of its research. ORD research programs also undergo formal performance evaluations by the Office of Management and Budget by way of OMB's Performance Assessment Rating Tool (PART). Additionally, the Board of Scientific Counselors, Science Advisory Board, National Academies of Science, and other advisory panels provide program evaluations that facilitate continuous improvement and ensure ORD is advancing the state of the science in key areas. Members of EPA's advisory boards are non-EPA scientists, engineers, and social scientists who are recognized experts in their fields. They come from academia, industry, government, research institutes, and non-governmental organizations throughout the United States. EPA chooses them for their demonstrated ability to examine and analyze environmental issues with objectivity and for their interpersonal, oral and written communication, and consensus-building skills.

In sum, ORD's research is guided by strategic directions and stakeholder input, adjusted according to annual budget decisions, evaluated to ensure effective and efficient management, and ultimately applied to inform environmental decision-making.

The Science to Decision-Making Continuum at EPA

Similar to other federal agencies that are required to produce both scientific assessments and regulatory decisions, EPA views the relationships between science, science-policy, and official Agency decision-making as a continuum.

To start, EPA science is conducted by individuals and teams working in our laboratories or in the field. All of their work is reviewed by subject-matter experts in accordance with EPA's highly regarded peer-review process and information-quality guidelines. Once an EPA scientific product meets scientific standards of quality and credibility, scientists are encouraged to publish and otherwise communicate their findings. Note that these independent, scientific findings do not necessarily represent official Agency policy positions, as national policies must also take other factors into account.

Science policy is an integral part of the continuum. Because the scientific method encourages critical thinking and professional disagreement, it does not commonly lend itself to a "bright line" that decision-makers can use as a reliable reference point. A range of reasonable and scientifically defensible options or decisions are usually available, and there is rarely a single "best answer" for use in decision-making. Scientific assessments also entail varying degrees of uncertainty and many decisions, choices, and assumptions must be made based on science-policy considerations.

To meet our statutory requirements, we often cannot wait for independent scientific findings to converge on a solution—this would cause long delays in environmental decision-making. Therefore, we rely on science-policy considerations, which often entail synthesizing and assessing a range of scientific opinions and data points. This process also involves filling in knowledge gaps in the body of technical information, and where necessary, using weight-of-evidence approaches to make scientific inferences or assumptions. The scientific models that inform most national policies require this kind of give and take. This work draws on expert insights from multiple scientific disciplines, and it is further strengthened by Agency, interagency, and public review.

Decision-making is further along the continuum. Science, however, is but one aspect of EPA's regulatory decisions. Other important considerations need to be factored into EPA's decisions without compromising scientific integrity, the Agency's mission, or statutory mandates. These considerations include technological feasibility, implementation costs, local autonomy versus federal control, justice, and equity. The impacts or limitations of these non-science factors, as well as the current state of the science, will influence how scientific considerations are brought to bear on environmental decisions facing the Agency.

Administrator Johnson and his leadership team give serious weight to science and science-policy choices in developing options for national policy. Nevertheless, the science to decision-making continuum does not end with regulation and rules. Every Agency decision feeds back into science and science-policy considerations as we monitor the effectiveness of our national policies and use updated information about changes in the quality of human health and the environment to adjust our policies over time.

EPA's Integrated Risk Information System (IRIS)

The IRIS program, which began in the mid-1980s, includes a repository of human health risk information on the potential adverse effects of long-term, or chronic, exposure to over 540 potential environmental contaminants. At the time the program was established, it was clear that the toxicity values that were being developed by EPA were not internally consistent across the Agency. For example, EPA's Program Offices were publishing toxicity values for a particular chemical in rulemakings and other policy documents that were orders of magnitude different. EPA developed these toxicity values using the same set of scientific data, but they were based on different human health endpoints or default uncertainty factors. Thus, EPA formed IRIS in response to a critical need to have Agency-wide toxicity values in one place. IRIS files included narratives detailing supporting studies, key assumptions, and choices. EPA health scientists developed and reviewed all of this information.

IRIS was originally intended to be an internal system that provided EPA risk assessors and managers with an EPA consensus position on the potential human health hazard and dose-response information for environmental contaminants of interest to Agency Programs and Regions. Word spread quickly about the existence of IRIS and many asked to make it a publicly available system. State and local public health and environmental agencies, as well as the regulated community, requested access to the IRIS information. Therefore, in the late 1980's, EPA made IRIS available to the public. EPA was pleased to share this information resource with a large, external user community. IRIS first became available on a dial-up service and later through the National Library of Medicine's TOXNET family of information resources, and then on the Internet. The IRIS Web site is currently accessed over 20,000 times per day with inquiries coming from over 100 countries.

Today's IRIS program presents a wealth of important information to decision makers and environmental managers. The risk information in IRIS can include quantitative risk estimates for both cancer and non-cancer effects. In addition, extensive narratives, or qualitative risk information, present a full discussion of the peer-reviewed scientific literature used in the assessment, the EPA confidence in the IRIS non-cancer risk estimates, and an explanation of the judgments (including application of default approaches and uncertainty factors) that the Agency must make in the face of inadequate data.

Risk Assessment and Risk Management

A significant part of EPA's mission to protect public health and the environment is to regulate, when necessary, the release of contaminants into the nation's air, water, and soil. As first outlined by the National Academy of Sciences (NAS) in its seminal 1983 report, "Risk Assessment in the Federal Government: Managing the Process," commonly called the "Red Book,"[1] there are two distinct steps that should be used in the federal government to assess and manage risks. These steps are *risk assessment* and *risk management.*

Risk assessment, as defined by the NAS, is "the characterization of the potential adverse health effects of human exposures to environmental hazards" (p. 18). Risk assessments can entail either quantitative or qualitative expressions of risk, and should include characterization of the uncertainties inherent in the process of inferring risk. The risk assessment process has four components: hazard identification, dose-response evaluation, exposure assessment, and risk characterization.

Risk management is defined by the NAS as "the process of evaluating alternative regulatory options and selecting among them" (p. 18). A risk assessment may serve as one of the bases of risk management.

An IRIS assessment is a risk assessment, albeit not a complete one. IRIS includes information on hazard identification and dose-response evaluation but does not include information on exposure and risk characterization. Government and private entities use IRIS—combined with exposure information, public health concerns, social considerations, as well as statutory and economic factors—to characterize the public-health risks of chemical substances and support risk-management decisions.

It is important to recognize that the risk-assessment process consists of both "science" and "science policy" components. This is an important distinction that is often overlooked, yet the 1983 NAS "Red Book" addressed this issue in its first chapter.[2] For example, conducting a toxicity study on animals in a lab is a science activity. In contrast, IRIS assessments must synthesize and assess a broad range of scientific findings and opinions.

The situation I referenced earlier, in which EPA Program Offices published different toxicity values for a particular chemical in spite of their access to the same set of scientific data, illustrates the distinction between science and science policy. In IRIS assessments, judgments and choices must be made about the most appropriate assumptions, data sets, health endpoints, and models to use in deriving toxicity values. These science-policy choices are important because the science alone is not sufficiently precise to provide definitive answers. For this reason, guidance documents such as EPA's "Guidelines for Carcinogen Risk Assessment" were developed and approved through the Agency's Science Policy Council to inform the many choices in the risk-assessment process.

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[1] National Academies Press, ISBN: 0309033497

[2] See page 28 and the section entitled "Scientific and Policy Judgments in Risk Assessment"

Revisions to the IRIS Process

The IRIS process has evolved over time in areas including the following: setting the annual IRIS agenda, level of independent/external peer review, and opportunities for public and interagency review. Because IRIS began as an internal EPA resource, the agenda for developing IRIS assessments focused on those chemical assessments of interest to EPA's Program Offices and Regions. Now EPA develops an annual agenda for the IRIS program and announces new assessments under review in the Federal Register. EPA uses five general criteria to determine which new chemicals to assess: (1) potential public health impact; (2) EPA statutory, regulatory, or Program/Region-specific implementation needs; (3) availability of new scientific information or methodology that might significantly change current IRIS information; (4) interest to other governmental agencies or the public; and (5) availability of other scientific assessment documents that could serve as a basis for an IRIS assessment.

In recent years, the IRIS Program has also sought nominations for IRIS chemical reviews from the public and other federal agencies. The list of new or updated assessments chosen for potential development is published in the Federal Register as part of the IRIS annual agenda. The Agency is also working to improve the prioritization process to more appropriately capture relative priorities of individual chemical assessments under development. EPA conducts an initial literature search for each of the assessments added to the IRIS agenda, and the results are posted on the IRIS web site (www.epa.gov/iris). At this point, EPA invites the public and other agencies to review the literature-search results and submit additional information to EPA.

Other recent changes to the IRIS process include creation of a chemical-assessment tracking system (IRISTrack) on the IRIS Web site to inform the public and stakeholders of the following: (1) the status of the IRIS assessments that are underway, (2) new opportunities for the public and other agencies to review and comment on the qualitative and draft IRIS assessments (including the ability to participate in "listening sessions" held during the public comment period), and (3) the availability of enhanced independent/external peer reviews of draft IRIS assessments.

The IRIS program has benefited from an expansion of scientific staff and a significantly increased budget over the last few years. Since FY 2003, EPA has nearly tripled the number of IRIS staff to 37.0 full-time equivalents. Through its FY 2009 request, EPA has also sought to quadruple the IRIS budget to $9.4 million.

In 2005, EPA initiated a formal process to document the steps in the IRIS process, including formalizing recent improvements to the process. On April 10, 2008, EPA announced the revised IRIS process—the first time in IRIS history that EPA has transparently documented the process and made it available to the public. Prior to the release, the IRIS process had often been viewed as a "black box" both within and outside of the Agency; it was unclear what steps comprised the process, what the timing was for each step, or where opportunities existed for internal and external involvement. Improvements to the IRIS process help define critical and appropriate roles for public and interagency comments and interactions, and promote greater communication and sharing of information between all interested parties and EPA. The revised IRIS process is designed to provide greater transparency, objectivity, balance, rigor, and predictability in IRIS assessments.

Delays in the completion of IRIS assessments have been a long-standing problem at EPA for a number of reasons, including the growing complexity of assessments, the lack of clear timeframes, etc. Prior IRIS assessments took an average of five years to complete, and EPA has been working on some assessments for a decade or longer. The revised process was designed to help address these delays, in part, by allowing for input from various stakeholders (e.g., EPA Program and Regional Offices, other agencies, scientific organizations, NGOs, the public) early in the process and providing clear descriptions and timeframes for each step. This approach helps EPA to collect necessary information while holding itself accountable to assessment timelines.

The early involvement of various stakeholders is consistent with recommendations from EPA's Science Advisory Board (SAB) as well as a prior report by the Government Accountability Office (GAO). In a September 26, 2000 letter to Administrator Carol Browner, SAB noted that "critical data" were often missing from IRIS risk assessments. SAB suggested that one way to enhance the quality of toxicologic evaluations was to "make the IRIS process open to public stakeholder review in a more formal manner." A 2006 report by GAO noted the following: "...several experts said that increased involvement with a broad range of stakeholders early in the planning process would help identify alternative methods and models and obtain stakeholder concurrence with the agency's approach."[3] The new process therefore allows the EPA access to a wide range of scientific data, expertise, and knowledge that can be used to produce timely and high-quality IRIS assessments. However, it should be noted that all draft IRIS assessments are peer reviewed by outside experts, and all final decisions on IRIS content remain with EPA.

It is also important to recognize that many of the assessments today are more complex than ever before. For example, some chemicals have extensive toxicity testing data that must be reviewed and analyzed; new data are now available for assessing the mode of action of many chemicals; and more sophisticated statistical and modeling techniques are now available. Considering the growing complexity of IRIS assessments, recent peer reviews of IRIS assessments by the NAS and EPA's SAB have recommended that EPA do a better job of incorporating quantitative uncertainty analyses. The timelines in the revised IRIS process allow EPA to address the additional information and analysis in today's complex assessments.

An important aspect of the revised process includes "mission-critical" chemicals that will be determined by a sponsoring agency together with EPA. A mission-critical chemical is one that is an integral component to the successful and safe conduct of an agency's mission in any or all phases of its operations. Agencies must identify to EPA's Office of Research and Development (ORD) those chemicals on the IRIS Program Annual Agenda that they determine meet this definition. They must generate a report documenting what types of new research will address significant data gaps and whether such research can be conducted within the allotted time frame. It is ultimately up to EPA to allow new research to be conducted. We do not anticipate that many chemicals will receive the mission-critical designation each year or that additional studies will be requested for all mission-critical chemicals. However, new studies could help fill important data gaps to ensure assessments of the highest quality.

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[3] GAO-06-595: "Human Health Risk Assessment: EPA Has Taken Steps to Strengthen Its Process but Improvements Needed in Planning, Data Development, and Training"

Independent, external peer reviews, which are described in more detail below, are another hallmark of EPA's commitment to ensuring high-quality science. Consistent with past practices, the revised IRIS process specifies that all draft IRIS Toxicological Reviews will undergo peer review by a panel of outside, independent experts. A small number of complex or high-profile chemicals may undergo more in-depth SAB or NAS peer reviews. As part of the revised IRIS process, external peer reviewers will also, for the first time, have an opportunity to review the revised IRIS Toxicological Review and comment on ORD's responses to the peer reviewers and public comments. This is an important step that is consistent with other peer review practices, such as publishing in the peer-reviewed literature, to reveal when peer reviewer comments are adequately addressed or sufficient rationale is provided for not addressing such comments.

The revised IRIS process meets many of the recommendations of the 2008 GAO report entitled "Toxic Chemicals: EPA's New Assessment Process Will Increase Challenges EPA Faces in Evaluating and Regulating Chemicals."[4] Specifically, the revised process (1) clearly defines and documents a streamlined IRIS assessment process; (2) sets time limits for all parties, including OMB and other federal agencies, to provide comments to EPA on draft IRIS assessments; (3) defines the appropriate role of external federal agencies in EPA's IRIS assessment process; and (4) determines the types of IRIS assessments to conduct on the basis of the needs of EPA's Program Offices and other users.

Although EPA's revised IRIS process addresses many of the recommendations, in the 2008 GAO report, it is our position that the report incorrectly characterizes of several key issues. The report suggests that only pure science is involved in the risk-assessment process. In reality, all risk assessments (including IRIS assessments) have always included a mix of science and science policy, as acknowledged in the 1983 NAS "Red Book."

The GAO report also mischaracterizes the interagency review process at EPA. Specifically, to ensure that scientists and policymakers are able to have full and frank discussions without being concerned about how these discussions may be viewed or misrepresented, all internal EPA comments and interagency comments, including disposition documents, on draft IRIS assessments are considered "deliberative" and do not become a part of the public record. This is not a new or unique process. This is the same protection allowed in many other policy-making settings at EPA, and other federal agencies follow similar processes. Moreover, once

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[4] GAO-08-743T

EPA comes to a conclusion and releases its external review draft, the assessment undergoes a transparent process of public comment and external peer review. The GAO report incorrectly suggests that EPA will not have the final say on the content of IRIS assessments under the revised process given the participation by other agencies. However, EPA's revised IRIS process makes it clear that all final decisions remain with EPA.

The revised IRIS process is designed to enhance the quality and timeliness of future assessments. EPA now needs time to implement and evaluate the new process.

Independent, External Peer Review

As indicated above, a practical and effective way that EPA maintains the integrity of its scientific programs and products is through independent, external peer review—the evaluation of Agency programs and products by panels of outside experts. EPA has a very strong peer-review program to ensure that only high-quality science is released and/or used by the Agency. Hundreds of Agency products undergo peer review each year, and nearly 90 percent are reviewed by independent experts who are not affiliated with the Agency.

EPA's Science Policy Council maintains our Peer Review Handbook, a "how-to" manual that is used by staff across the Agency. In addition, external stakeholders often refer to the Handbook as a model of strong peer-review practices, which include: peer review by experts who are independent of the Agency; public review and comment as appropriate; and maintenance of transparent, public records of scientific products at relevant stages of development. Our updated Peer Review Policy (2006) and 3rd edition of the Peer Review Handbook (2006) benefit from insights gained by implementing the program over the last decade. The 2006 Handbook clarifies ethical standards in order to improve understanding and compliance on the part of staff and management.

Our peer-review program fits within the context of a larger, Agency-wide quality system. EPA's quality system is the means by which we manage our scientific information in a systematic, organized manner and it provides a framework for planning, implementing, and assessing EPA's scientific work. Our peer-review policies also incorporate the provisions of the Office of Management and Budget's (OMB) Final Information Quality Bulletin for Peer Review. This Bulletin contains provisions for conducting peer review at all federal agencies in order to enhance transparency and accountability and applies to "influential scientific information" and "highly influential scientific assessments." OMB's Information Quality (IQ) Guidelines, together with our own IQ guidelines, are important elements in our quality system, as required by Congress in what has become known as the Information Quality Act.

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The cornerstone of the external peer-review process is the peer reviewer, the individual scientist or other expert who graciously agrees to take on the responsibility of closely and impartially examining EPA research programs and results. Identifying and selecting potential peer reviewers are critical components of a credible peer-review process. A clearly demonstrated high level of expertise in the appropriate field is a minimum qualification. In addition, potential or perceived conflicts of interest must be disclosed to allow agencies to make informed judgments about the appropriateness of each reviewer. For example, direct financial gain is an obvious source of conflict of interest. Other examples include a professional stake in an issue, illustrated by serving as an expert witness or advocating for a particular view on the topic subject to peer review.

While disclosure of a potential or perceived conflict of interest is not necessarily grounds for keeping a potential reviewer from participating, failure to disclose certainly is. This issue becomes especially troublesome when the failure to disclose becomes known once the peer-review process has begun or been completed.

EPA, like other federal agencies and credible scientific bodies, has gone to great lengths to ensure that all potential or perceived conflicts of interest of peer reviewers are disclosed during the selection and review process. For example, questionnaires have been developed that seek to identify all potential issues, and peer reviewers are asked to certify their answers during the initial process and again before the review begins. It is important that reviewers take these questions seriously and respond completely so that an unnecessary and potentially embarrassing disqualification does not take place.

The peer review of assessments, which often synthesize multiple scientific studies, may include a number of steps: internal peer consultation, intra-Agency (internal EPA) review, interagency review, and independent/external peer review. For example, to enhance the quality and transparency of EPA's IRIS assessments, the revised IRIS process specifies that each Toxicological Profile undergo peer review as follows:

- Internal Peer Consultation: Internal (EPA) peer reviewers are selected to provide detailed scientific feedback on the draft assessment.
- Intra-Agency Review: The draft assessment is reviewed by a standing group of senior health scientists representing EPA's Offices and Regions and by selected senior health scientists with scientific expertise relevant to the substance under review.
- Interagency Review: The revised draft assessment is distributed through the Office of Management and Budget for review by scientists in other federal agencies.
- External Peer Review: EPA obtains external peer review, typically via a panel meeting that is open to the public. At this time, the draft assessment is posted on the internet for public comment. EPA may submit more challenging assessments to high-level advisory panels, such as the EPA Science Advisory Board or National Academies of Science.

Peer review is also conducted at a higher level of planning and management, as discussed previously in the section on Science Planning and Management. For example, EPA's Science Advisory Board, among other bodies, reviews the Agency's research strategy and programs. SAB reviews provide critical cross-Agency perspectives as EPA establishes its research priorities in the near and long-term. Additionally, EPA ensures systematic, external peer review of research programs in its Office of Research and Development (ORD) by the Board of Scientific Counselors and others. Each ORD research program undergoes a detailed review approximately every four years, with a mid-cycle review after two years. These external perspectives promote continuous improvement and help EPA to focus on the highest-priority research needs to protect human health and the environment.

Conclusion

Thank you, Chairman Stupak and members of the Subcommittee for this opportunity to discuss scientific integrity at the EPA, the IRIS program, and our rigorous peer-review process. I look forward to answering any questions you may have.

Mr. STUPAK. Thank you for your testimony. Let me ask you this. Page, it looks like 5, on your testimony, you say once an EPA scientific product meets scientific standards, you go on, you say note these independent—I am trying to find the part here where you said about they get to communicate. You said something about you hope that they communicate their findings, right?

Mr. GRAY. Yes.

Mr. STUPAK. Once an EPA scientific product meets scientific—scientists are encouraged to publish or otherwise communicate their findings. So why would you remove Dr. Rice then if she is communicating her findings to the Maine Legislature?

Mr. GRAY. Well, I was here for a large part of the last panel and it is clear to me that there is a lot of confusion about the situation with Dr. Rice. What I would like to do——

Mr. STUPAK. Well, you removed her, right?

Mr. GRAY. No, she was not removed. The peer review had already taken place. What I would like to do is to——

Mr. STUPAK. The peer review had already taken place. OK. So why did you redact her testimony and take it offline?

Mr. GRAY. That is why I would like to call your attention to a letter that was sent by the Agency, signed by Chris Bliley, who is the director of our Office of Congressional and Intergovernmental Relations, to the chairman of the full committee in response to several of his questions, and it lays out the situation with Dr. Rice. The first thing that I want to say is that we have a great deal of respect for Dr. Rice and for the work that she does and her scientific expertise. It is why she was chosen as or was a potential member of one of our peer reviews. But we have very specific rules that we follow in our peer review. As——

Mr. STUPAK. Now wait. Do you have rules or do you have guidelines? What are we talking about here? Or is this the pirate code?

Mr. GRAY. This is back to our discussion of the arm's-length relationship that we have with contractors who do our peer reviews. Those contractors do have a series of questions that are asked of each of the members of the peer review panel, partially to establish things like conflict of interest, to establish expertise, and things like that.

Mr. STUPAK. Right. So the independent contractor didn't find any conflict of interest of Dr. Rice because they put her on the panel, right?

Mr. GRAY. The potential peer reviewers are asked to answer a series of questions and then just before they get together again as a peer review panel, they are asked the questions again.

Mr. STUPAK. OK. Was that done in this case?

Mr. GRAY. This is about——

Mr. STUPAK. Was that done in this case?

Mr. GRAY. Yes, it was.

Mr. STUPAK. OK.

Mr. GRAY. And disclosure is a very important part here. We look for expertise, and if there are potential conflicts, we want them to be disclosed. The Agency does not make a determination about potential conflicts, the contractor does, but they need good information to do that.

Mr. STUPAK. So the contractor made the decision to seat Dr. Rice?

Mr. GRAY. In this particular case——

Mr. STUPAK. I don't want you to filibuster me. I am trying to ask a question.

Mr. GRAY. OK. In this particular case, let us come to the crux of this issue.

Mr. STUPAK. Let us get right to it.

Mr. GRAY. Dr. Rice was asked just before the peer review panel got together, "have you made any public statements or taken positions on this or other subjects closely related to the chemical or topic under review?" She was asked this question on February 16 and said no.

Mr. STUPAK. OK.

Mr. GRAY. And February 15 was one of her testimonies before the Maine Legislature, so we were in a situation in which our contractor did not have the full disclosure to be able to make their judgments——

Mr. STUPAK. And did you realize that what she testified on the day before was not about deca?

Mr. GRAY. "Have you made any public statements or taken positions on or closely related to the subject chemical or topic underway?"

Mr. STUPAK. Right. And the day before, what did she testify to or talk to the working group in Maine on?

Mr. GRAY. She talked about exactly the chemical that was the topic under review.

Mr. STUPAK. You are sure of that?

Mr. GRAY. Yes.

Mr. STUPAK. OK.

Mr. GRAY. Our judgment in this case, and this was a judgment that was made by the staff-level folks who run our National Center for Environment Assessment. They are the ones who made the judgment that——

Mr. STUPAK. So what did she testify to on February 15 about deca before the Maine working group?

Mr. GRAY. The subject of her testimony is not what is important here. What is important is the fact that it wasn't disclosed to us so that we could not make an appropriate decision——

Mr. STUPAK. Wait a minute. Did she testify about deca on the 15th? If so, what is it she said that would violate that standard?

Mr. GRAY. According to our letter to the chairman, Dr. Rice had testified on February 15 before the Maine Legislature in support of a state ban of deca bromodiphenyl ether, or PBDE.

Mr. STUPAK. OK. And I think Dr. Rice testified at the last panel that is not what she testified to. They talked about a safer substitute. She never reached——

Mr. GRAY. You have to have a substitute for something.

Mr. STUPAK. Pardon? If her testimony is talking to a working group of the Maine Legislature and they are asking about deca and they are talking about are there safer substitutes, how is that a conflict?

Mr. GRAY. This is not about a conflict. This is about non-disclosure of having made public statements or taken positions on this or other closely related subjects, and in this case, when this came to light, the decision was made by the director of our National Center for Environmental Assessment——

Mr. STUPAK. Well, Dr. Rice is still here. Dr. Rice, do you mind coming back up and I will ask you testify on this? Because I think there is a lot of confusion. I want to get this cleared up.

Ms. RICE. I kind of wish I had left.

Mr. STUPAK. First of all, I have to remind you, you are still under oath, Dr. Rice, still under oath.

Ms. RICE. Yes.

Mr. STUPAK. So on February 15, did you testify before the Maine Legislature about deca?

Ms. RICE. I testified to one of the committees.

Mr. STUPAK. Pardon?

Ms. RICE. I testified to one of the committees of the Maine Legislature.

Mr. STUPAK. OK. Testified on what?

Ms. RICE. On the Maine bill, which had a presumptive ban for deca BDE on the provision that safer alternatives were available.

Mr. STUPAK. And was it about safer alternatives or was it about deca and if it was bad or good or should be banned?

Ms. RICE. It was really about both in that my concern was whether I could really say that the safer alternatives were better, whether the potential alternatives were safer than deca. So I really had to in some ways compare and contrast, and what I indicated to the committee was that we didn't know enough about the toxicity of the alternatives. We had limited information on the toxicity of deca, which was the subject of the peer review, but we did know a lot about the persistence and biocumulative properties of deca.

Mr. STUPAK. So when you answered the question the next day, did you feel it was wrong, that you failed to disclose?

Ms. RICE. Well, in retrospect, I probably should have said that I had testified to the Maine Legislature, but in my mind, the two exercises, the two topics were completely separate because derivation of a reference dose is a very limited exercise and it talks only about the hazards, it talks only about the toxicity and not about the other properties, and really I was talking about the other properties, so I considered that I hadn't said—I certainly never said anything about my opinion about what the reference dose of deca should be or—and we keep talking about deca but in fact there were four chemicals and I never talked about the other three chemicals at all, and so in my mind at that time, the two things didn't have anything to do with each other. In retrospect, I would have put it on the form.

Mr. STUPAK. Before they pulled down your statement on the Web site, did they inform you why they were taking down your testimony and your findings?

Ms. RICE. Well, I got a telephone call from Dr. Gray and didn't take notes, so it is hard to remember a year-and-a-half later exactly what was discussed. But he told me that they had gotten this letter from the ACC and he asked me questions about the form and—well, not the form specifically but the timeline, when I had testified and what had happened when, and then he indicated to me that he was actually thinking about removing me from the panel, and I have to say that I was so surprised by that that a lot of the rest of the conversation just went out the window.

Mr. STUPAK. Dr. Gray, page 5, you go and you say, "Because the scientific method encourages critical thinking and professional disagreement, it does not commonly lend itself to a bright line that decision makers can use as a reliable reference point." It seems to me you are using a rather bright line here to exclude Dr. Rice.

Mr. GRAY. No, sir, I am not. The decision was made on Dr. Rice, it was made by our National Center for Environmental Assessment, and I did support it, was that because the disclosure rules had not been followed, it was inappropriate for her comments to be part of that record simply because our contractor did not have the information they needed to make an appropriate judgment. If she would have disclosed this, I am guessing that she probably—the contractor would not have changed the situation, would not have had anything to say about her position on that board.

Mr. STUPAK. So even though the other four people on this peer group agreed with Dr. Rice or they all came basically to the same conclusion, that is not the issue here in your mind, it was just that she didn't disclose this meeting with the Maine Legislature?

Mr. GRAY. I am glad that you have really exactly identified the issue. This is not a situation about——

Mr. STUPAK. Yes, I did, and I can't believe you would disqualify her on that.

Mr. GRAY. This is about process. If we have a process that cannot be trusted, when we tell people, we ask all of these conflict of interest questions and we don't have—we can't tell them that we have confidence that those are being answered——

Mr. STUPAK. A process that can't be trusted with this IRIS program where you have OMB and things are done in secret, there is no transparency, that is a process that cannot be trusted.

Mr. GRAY. No, that process, remember, comes back to the peer review that we both support very much. There is no way for other federal agencies or anyone to play scientific shenanigans with the IRIS process when it has to go through a peer review process by independent expert peer reviewers at the end.

Mr. STUPAK. Do you want to put up the last one?

[Chart shown.]

Mr. STUPAK. So where is the—I am looking at the IRIS process, the latest one, post April 10. I am on 12A. OMB interagency review and approval. I don't see anywhere in there where there is a public review of that, goes right to the EPA and final rule is made, so where is the transparency, where is the peer review of the OMB interagency review and approval in 12A of your IRIS process?

Mr. GRAY. In this case, this is simply the end of the process. It has been through peer review, and this is the final——

Mr. STUPAK. Right, and that is done in secret. OMB stuff isn't disclosed. I think the record has very clearly been established.

Mr. GRAY. No, it is very much like the way we do our internal agency reviews where we don't share the comments that we get from other parts of EPA either, and here you will notice the very last line of section 12 is of course that the final decision on IRIS rests with EPA.

Mr. STUPAK. It is already done by then.

Mr. GRAY. We make the final decisions.

Mr. STUPAK. Based on what you heard from the Administration, which is OMB, which deliberations are in secret, we have established, right?

Mr. GRAY. I am sorry.

Mr. STUPAK. Your final decision is based upon recommendations from OMB, which is the Administration, and that is a secretive deliberation.

Mr. GRAY. It is EPA's decision. That is the important point.

Mr. STUPAK. My time is up. Mr. Shimkus for questions. We will come back to this panel.

Mr. SHIMKUS. Thank you, Mr. Chairman. Don't come back up to the table, Dr. Rice. Again, I think, I know I have been caught in a bureaucratic, legalistic period of time and I just apologize for this, and unfortunately, people end up getting caught up in messes like this because of our rules and regulations and the like. You know, the hearing is trying to prove political attacks on the scientific community within the EPA and I understand the intent of what we are trying to do. I don't think there is going to be success. There is frustration and I share the frustration of the handling of your case, and the reality is, I had an ethics issue, and I got called in for 3 hours with attorneys going over what I said, what I didn't say and all this other stuff, and you just can't win. They start splitting hairs so much that people get hurt. So again, I just do it to apologize and that is sometimes what happens here in a legalistic environment. That is why I am not a lawyer and I am never going to be one.

The issue is more clarity. Let me talk about how do we—here is another example from politics is, there will be times when a reporter will ask us, can we get you to speak not for attribution. That means can you speak clearly, and we are not going to attribute that to you so we can get the truth. We have reporters back there. They know. They like us to do that sometimes. So my sense is, sometimes in this process, you want to have scientists in a room where they can speak not for attribution, so they can fully say what they want to say in this analysis and then put it together and share that. Dr. Gray, is that along the same lines?

Mr. GRAY. That is a very, very good description of the situation that we go through, not just within the Agency where we have those same kinds of discussions and they are not always just holding hands and agreeing but also in the interagency process, and we believe that that ultimately makes our product stronger. We are getting scientific input, scientific expertise from a variety of different experts that we think makes our product better, and then at the end, the important thing again is that that product has to go through an independent peer review and pass muster with the scientific community.

Mr. SHIMKUS. And that is how really how—because the follow-up question is, how do you balance, and so you would say you balance it by the independent peer review?

Mr. GRAY. And we get independent peer reviews and not infrequently that will come back and tell us we don't think you did this right, go back and do it again, so that even with the best process that we can come up with, there is still often scientific disagreement and it is what makes this process strong. We can go back, do it again, and learn from the scientific input.

Mr. SHIMKUS. Now, based upon the other panels and stuff, when we are talking about peer reviews, either internal peer reviews or other agencies' reviews and if there are other agencies, are you able to see—there is always a great receptivity to transparency. Politicians use it all the time, bring the sunlight on, it sanitizes the system. Of course, we know that we don't always use that, an example again with the media. You want to have confidential discourse so you can fully lay out the case. Talk about the peer review, internal and external.

Mr. GRAY. OK. Well, we think that the process, this new IRIS process really does allow greater opportunity for broader participation by all stakeholders, not just at other federal agencies. We have more opportunities for the public to be involved, more opportunities for the rest of EPA to be involved when we are developing IRIS profiles. We go through that process with articulated time frames, which has never been in the IRIS process before that says how long steps are going to take and then we go into these various forms of review. We have review within the Agency. This is followed by interagency review followed by public review and peer review. All of those are ways in which we strengthen our process. If there is some specific things about the peer review process that I can answer——

Mr. PEACOCK. So for clarity, the internal review and the interagency review is confidential. You can call it secret or black box but the fact is, it is confidential just like a peer review at a scientific journal is confidential so that you can have a free flow of ideas and exchange within the scientific community, make sure the product at the end is as strong as possible. It is not an unusual idea.

Mr. SHIMKUS. Right, but then of course the other flip side would be, how do we ensure that the public has confidence in the product?

Mr. PEACOCK. And my answer there then comes back to that independent peer review. When EPA is done with its process, we have talked to our agency, other agencies, we have comments from the public. We give that to independent peer reviewers who are again arm's length, not chosen by us, and ask them to review the work that we have done. If there is funny business that is being tried, if there are interpretations that are not scientifically tenable, if there are decisions that are being made that don't have scientific support, we will hear that back and the public can be confident in fact because of this independent scientific peer review.

Mr. SHIMKUS. Let me just add two comments. One, the time frame thing sounds good, but the record on our ability to move does not support the fact that this is an efficient system that gives a timely response, and you are going to find me defending that. Do you want to comment on that?

Mr. PEACOCK. Yes, I would like to comment on that. One of the things I focused on as the chief operating officer is making sure people can see how EPA is performing. We are the first agency to have quarterly performance measures we make available to the public. We are going to put on this report how quickly we are now doing IRIS reviews compared to how quickly we have done them in the past, so everybody, every 3 months is going to be able to see whether or not we are going to deliver on what we have said we are going to deliver on, which is faster IRIS reviews and keep the quality up.

Mr. SHIMKUS. So you are going to tell me that this system is going to be quicker than this system?

Mr. GRAY. Well, sir, I think—well, if you look right now at the average of the IRIS assessments currently underway is 5½ years, and we have some that have been going on for 10 years, 15 years, because we have never before had a process written down with timelines that hold our agency accountable, that hold other agencies accountable, that hold the peer review process accountable. That is what we have written down there and that is what the deputy administrator has asked us to find a way to report out to the public to demonstrate how we are doing meeting our goals, if there are problems, where they are, are they coming from the interagency process or are they coming from the public process, are they coming from our own work. We are trying to open this up.

Mr. SHIMKUS. We would love to see that. We would love to see these reports so that we can then say, hey, the system is really working.

Mr. GRAY. Or if not, why not.

Mr. SHIMKUS. Yes, which right now we are not assured, but hopefully we will be. The backlog, will it be prioritized?

Mr. GRAY. We are working through a number of ways in which we identify the best—how we set our agenda for each year and out the people and the resources that we have in the IRIS program to work. We are consulting more broadly than we have before with the public, with other federal agencies, and with others to find out what are the highest priority compounds and we will move those forward. We have put significant increases in resources both people and money into the IRIS program over the last 4 or 5 years and we are trying to make it work.

Mr. SHIMKUS. I am not going to be silly, but is that open for public comment?

Mr. GRAY. Yes, it is. Step one, we publish an IRIS agenda in the Federal Register every year and you are very welcome to tell us what you think are the highest priority chemicals for us to work on and that goes into part of our process.

Mr. SHIMKUS. If that is the case, then that is great because hopefully we get the worst ones first, I would assume.

Mr. Chairman, that is all the questions I have. Thank you.

Mr. STUPAK. Well, thanks. I have a few more questions.

Kyle, put up that flow chart again, the post April 10.

[Chart shown.]

Mr. STUPAK. Dr. Gray, you said that, I think I quoted you right, you have independent scientific peer review in this process. The only place I can find that is number 9 way up there in the top, and then right there, 10A, independent. OK. But then OMB comes back in at 12A. So the independent peer review and comment, when the Agency, EPA, makes its final decision after it gets its input from OMB, there is no review of that decision. You do it and then you go back into secretive or your closed interagency review.

Mr. GRAY. Well, you will notice that in fact that splits there. There is something we do to maintain the value of our peer review process.

Mr. STUPAK. Don't tell me you have another box you want to put in there.

Mr. GRAY. It is a new step that we have put in there where we send our response to their comments and a revised document back to the peer reviewers and we ask them to comment, how have we done——

Mr. STUPAK. So at 12A, you send it back to 10A?

Mr. GRAY. No, you can see that it splits. In parallel, we are asking our peer reviewers to say how we did with your advice because we have had a lot of concern that though we do this internal peer review, we don't take their advice. This way these advisors do not have an opportunity to——

Mr. STUPAK. OK, it splits there, 12A and 12C, that is what you are talking about the split, right? Are you trying to tell me you bypass OMB? If you don't go 12B, you go 12C, right?

Mr. GRAY. I am saying that our revised final document also goes out for scientific review as well to ensure that the way in which we have addressed——

Mr. STUPAK. Yes, but the order is already done.

Mr. GRAY. What is that?

Mr. STUPAK. The order is done. Your final EPA clearance, you have already issued the order. Sure, the science community can comment on it then, but it is a little bit too late, the horse is out of the barn by the time you get a chance to review it one more time. Go ahead.

Mr. GRAY. The idea here is that when we have taken all of these comments into advisement, we have revised our document. We have written another document that says here is the comment we got and here is why we either took or didn't. We send that as part of the final document that is going back to the interagency process. We also send that out to the peer reviewers, and we are asking them, how did we do on our science.

Mr. STUPAK. So that is 12C, right? That is 12C is what you are talking about?

Mr. GRAY. No, that is when it goes to the EPA group to look at as well. One of the things that——

Mr. STUPAK. Give me the number. Where does this occur in your flow chart here? After the last time the OMB gets their hands on it, when does it go back for this independent scientific peer review? Tell me that on this flow chart.

Mr. GRAY. Well, it is another peer review. It is another opportunity for the peer reviewers to comment on how we have done with their scientific expertise.

Mr. STUPAK. Where does that occur on this goofy flow chart?

Mr. GRAY. That occurs—well, these flow charts are something that I can't endorse. I did not put these together so I am not sure how those work.

Mr. STUPAK. Neither do we. That is why we are asking the questions. I don't think anyone understands how this thing works. This came from you. This came from the EPA.

Mr. GRAY. No, but that—well, the document that was part of the memo that came out announcing this is the place that to me gives us the best review of the process, and it is in step 11.

Mr. STUPAK. Step 11. OK, 11, there we go, but see 12A now, you have OMB back in there, and if you want to split it like you said, go to 12E, you get OMB in there again. OMB gets about four bites of the apple for secretive deliberations that we don't get to know about. Let me ask you this though. You mentioned timelines. If I start request for chemical nominations for IRIS, until I get to 13D, post final assessment on IRIS, what is my timeline? How is it going to take me?

Mr. GRAY. Depending on, because all of these are ranges, somewhere between 3 and 4½ years.

Mr. STUPAK. Three and 4½ years?

Mr. GRAY. Yes. The current average is 5½.

Mr. STUPAK. OK. GAO says it is 6 to 8, so your average would be 7.

Mr. GRAY. They might want to check their math.

Mr. STUPAK. Or is that the new revised one since post April 10?

Mr. GRAY. There is nothing revised since April 10.

Mr. STUPAK. Yes, your revised process, IRIS process.

Mr. GRAY. No, that was the process that was released on April 10.

Mr. STUPAK. All right. So dioxin, we have been waiting since 1991. When can we expect that one to be done?

Mr. GRAY. Dioxin is a terrific example of both why we need a better process.

Mr. STUPAK. Well, we are on our third draft of this process.

Mr. GRAY. You know why? Because we went to the National Academies of Science with our last draft and they said you have not done your science right. That is a problem. You need a process to make sure we are doing the science correctly——

Mr. STUPAK. With your new revised process, which has all the science so great, when can we see something on dioxin? We have been waiting since 1991.

Mr. GRAY. Dioxin is entering into a process and the amount of time it will take we are hoping is in that 3 to 4½-year process.

Mr. STUPAK. So another 3 to 4 years?

Mr. GRAY. I am afraid so. We were told by the National Academies that we had a lot of work to do.

Mr. STUPAK. Has National Academy approved this flow chart?

Mr. GRAY. Oh, no, no, they are occasionally used as one of our peer reviewers on very high-profile chemicals——

Mr. STUPAK. How about TCE?

Mr. GRAY. There is another one. We went to the National Academies and they told us that they didn't agree with our interpretation of the science.

Mr. STUPAK. Right, and they took 2 years, they came back with a report so now——

Mr. GRAY. We are now expecting to have the draft report ready by the end of this year.

Mr. STUPAK. Draft report. Then how long are you going to sit on it before it is a final report?

Mr. GRAY. Our expectation is to meet the timelines that are within the new process.

Mr. STUPAK. So what is the timeline after you get a draft report? How much time do you have then to issue a final report?

Mr. GRAY. I haven't done the math from individual parts in this process but it will then go through this process——

Mr. STUPAK. So there is not a timeline like 60 days, 90 days, 180 days, is there?

Mr. GRAY. Yes.

Mr. STUPAK. Well, why can't you tell me the time then?

Mr. GRAY. The document here that was released describing the process has timelines for each step. Again, that is something that didn't exist in the past and that we have put down to keep accountability both for our work and for the other parts of the process.

Mr. STUPAK. I agree, and I don't think anyone can understand it. Let me ask you this. Has there ever been an instance where someone forgot to disclose something on the disclosure form but were not removed from the peer panel?

Mr. GRAY. Not to the best of my knowledge.

Mr. STUPAK. How many other instances have you removed someone for an oversight on the disclosure form? Did you ever do that before?

Mr. GRAY. I don't—not to the best of my knowledge, and again, this was a decision that was—this was made by our IRIS staff and I supported it, but this was——

Mr. PEACOCK. Chairman, that is probably something we can research and get back to you on.

Mr. STUPAK. All right. Well, after you redacted Dr. Rice's name and comments from the deca peer review panel comments, you later posted a version with her redactions, but you also put a disclaimer on indicating she was removed due to a potential conflict of interest. It is Exhibit #14 right there in the binder. Why would you do this disclaimer? Why not just redact it? Don't you think you cast aspersions on Dr. Rice by saying she had a conflict of interest that wasn't disclosed?

Mr. GRAY. And Mr. Chairman, you are right, and Mr. Shimkus was right on this too. This is a situation that was very, very difficult for us. As I said, we have great respect within the Agency for Dr. Rice and for the work that she has done. She is serving a very valuable service to the Agency, but we also have a situation in which we have got one of our very specific rules and steps that hasn't been followed. And I may not have described that in the best way.

Mr. STUPAK. Well, if you have so much respect for Dr. Rice, and I believe you do, so she made an oversight and her conclusions were supported by the other four people on this peer review, they all reached the same conclusion, including the industry person who was on there who was pro-industry, why did you go through all this then? Why didn't you just say to ACC, we are sorry that there was this oversight but you know, we have known her for 30-some years, she worked at the EPA, she is the toxicologist for the State of Maine, I can see why she talked to the legislature, the conclusions are the same. Isn't that what is important in this thing, the conclusions that this panel came up with?

Mr. GRAY. It is also important to have a process with integrity that people can trust, and as I said, this was a very, very difficult situation and a very difficult call but we believed that having a situation in which we knew some of the important rules for disclosure, which are important to us being able to have our peer review process hadn't been followed made it——

Mr. STUPAK. Were you here when Ms. Kneiss testified on behalf of the American Chemical Council?

Mr. GRAY. No, I was not here for her testimony.

Mr. STUPAK. Well, she said the whole process was flawed. She said their concern was that whole process was flawed. So why wouldn't you just take down the whole peer review and not have them on the Web site?

Mr. GRAY. Because we didn't want to start over. We felt that this was a way to continue to move our timelines forward, to do the work the right way so that it was an appropriate response in the middle of this process.

Mr. STUPAK. As you are selecting these peer review panels, do you need ACC's permission or approval of the people who are going to be the peer reviewers on these panels?

Mr. GRAY. Well, first of all, we don't select the peer reviewers.

Mr. STUPAK. I know. You have the——

Mr. GRAY. No, our contractor doing that at arm's length is a very important thing to the integrity of the process.

Mr. STUPAK. Do you need the industry's approval before you do this? Does that independent contractor who picks the peer reviewers, do they need industry's approval?

Mr. GRAY. No, they make these decisions independently.

Mr. STUPAK. Exhibit 6 in the book there is ACC's letter to EPA asking for Dr. Rice's removal. Prior to this letter, has EPA ever received a letter from industry calling for removal of a peer review panelist? Is this the first time you have ever seen one of these where industry comes and says remove this person?

Mr. GRAY. In my experience, I believe this was the first one I had seen.

Mr. STUPAK. OK. Do you believe that the science, there is uncertainty related to individual studies and a judgment call to be made with regard to the weight of the evidence given to that science?

Mr. GRAY. I am not quite sure of the question, but of course, there is always uncertainty in science in the way that we want to apply it, yes.

Mr. STUPAK. Sure. OK. I have no further questions. Mr. Shimkus?

Mr. SHIMKUS. Thank you, Mr. Chairman, and I will be brief.

Dr. Gray, do you know if Dr. Rice is on a panel right now?

Mr. GRAY. I don't know.

Mr. SHIMKUS. Are you? Sorry.

Ms. RICE. That is OK. Subsequent to serving on the PBDE panel, it really wasn't just a deca panel, I later served on a peer review panel for thallium.

Mr. SHIMKUS. Great. Thanks. Again, I think this has been educational for a lot of us who aren't in the scientific community. Dr. Gray, in your long scientific career, you have had disagreements with scientists who have worked with you in the past, I am assuming. Is that correct?

Mr. GRAY. It is unusual to find unanimity among any group of scientists larger than one.

Mr. SHIMKUS. So how does a supervisor walk the fine line between engaging in scientific debate with staff who disagree and who may think that the debate is an attempt to influence them?

Mr. GRAY. One of the things that we really encourage and one of the strongest core values of EPA and especially the Office of Research and Development in our science and technology arm is that this open debate and open sharing of scientific information is the best way to serve the Agency, to serve the public.

Mr. SHIMKUS. Is it important for supervisors to challenge staff?

Mr. GRAY. I think that it is important for—in many ways, it may not be the role of the supervisor although supervisors are there to make sure that people are doing the work they are supposed to be doing in the appropriate ways and then that work has to go through, as our products do at EPA, through some sort of peer review to check on their scientific quality.

Mr. SHIMKUS. On the flip side, is it important for staff to challenge supervisors?

Mr. GRAY. I think what you learn in science school is, it is important to ask questions no matter who you are asking them of.

Mr. SHIMKUS. Yes, and I would agree, and I know sometimes we don't like to get in those debates and discussions. I think that is all the questions I have, Mr. Chairman. Thanks.

Mr. STUPAK. Just a couple for Mr. Peacock. Mr. Peacock, the report there by the Union of Concerned Scientists, you must have seen the report, right?

Mr. PEACOCK. Yes.

Mr. STUPAK. What did you think of the report? You had 800 and some scientists, 500 and some said they felt political pressure.

Mr. PEACOCK. I have three things to say about the report. First of all, I was concerned about it. We don't tolerate political interference with science at the Agency, just like we don't tolerate manipulation of peer review panels. So I took a serious look at it. The second thing I would say about it is, it didn't take too long for me to find what I thought were a number of fatal flaws in the report and I am sure they are not complete, and some of them I think have been mentioned today, including the response rate. Most of the—over a third of the respondents do not do scientific duties as the main part of their job so I don't know why we are calling them all scientists. There are issues regarding the wording of the questions themselves. Undue delays in a Web site or a press release being released is automatically considered political interference, so I didn't put a lot of faith in the report. It still concerned me, so then I thought, well, what other signs would I see if there was political interference, and I just don't see those signs. I do all-hands meetings as the administrator does with almost all the offices in EPA every year. This is not an issue that comes up frequently. Rarely, if at all, I would say. EPA is one of the top 10 places to work, has resulted in that way due to surveys consistently year after year, so I don't get the sense—and we have a lot of scientists. I don't get the sense that people are actually seeing that.

Mr. STUPAK. In these yearly surveys, do you ask about political pressure?

Mr. PEACOCK. It is a survey done by OPM and they ask a lot of questions about how people feel about the workplace, about their supervisors, about benefits, and it is not an issue that comes up.

Mr. STUPAK. Is it just yes and no on these surveys?

Mr. PEACOCK. I don't know. I am only familiar with the results where they rank the agencies and we are always in the top 10.

Mr. STUPAK. So you don't know anything about the survey, if they even ask about pressure from supervisors or——

Mr. PEACOCK. They ask about the relationships with supervisors, and I don't—they certainly don't go over the specificity of political interference on questions of science.

Mr. STUPAK. Let me ask you this. Dr. Gray says in his testimony on page 4 about the risk assessment process that, and I am quoting now, "The criteria for transparency were written to ensure that the public"—I am talking about IRIS now—"that the public would understand all the steps, logic, key assumptions, limitations, and decisions and the assessment process and also comprehend the supporting rationale that led to a particular decision or outcome." Now, to accomplish these lofty goals, don't you agree that the Agency comments provided to OMB then should be made public along with OMB's comments?

Mr. PEACOCK. No, I don't, and it goes——

Mr. STUPAK. Aren't you contradicting that testimony then?

Mr. PEACOCK. Well, I go back to Mr. Shimkus's point. There is a balance here, and you see this throughout science of people having the ability to have a fair and honest discourse about a scientific product which involves policy judgment and then also at some point having them come into the light of day and have to withstand the crucible of public review, and to me, this process strikes a balance.

Mr. STUPAK. So what is more important, OMB or public review and comment?

Mr. PEACOCK. They are both important. The reason IRIS exists is because there is disagreements between agencies on what the right level—FDA may want to set one level and EPA another. We have to speak with one voice and OMB has the responsibility to bring those agencies together and find what that one voice is.

Mr. STUPAK. Kyle, go to the first IRIS one, the pre-2004, the simple one. OK.

[Chart shown.]

Mr. STUPAK. OMB had one input in that one, and that was, they were involved one time. Under the new process, OMB gets involved on three separate times. Kyle, go to the last one there, the post-April 10 one.

[Chart shown.]

Mr. STUPAK. So what special scientific knowledge does OMB bring to the process that EPA, its advisors, and peer reviews don't have that they go from one time into the process, now they are in three times and they have the last say on it. So what special knowledge does OMB bring that EPA and its advisors and peer reviewers don't have?

Mr. PEACOCK. It is OMB's responsibility to bring the federal agencies together to come up with one answer, and that is the deal with IRIS. You have to have one answer. So scientists from whatever agency——

Mr. STUPAK. Was OMB failing to do that prior to 2004, bringing it together?

Mr. PEACOCK. No, the problem with this process, which I think the GAO report certainly highlights and that you have highlighted, is, we don't get these—there was never a process laid out and we don't get these reviews done very quickly. In fact, they are done very late. They are very slow. So for the first time, and I give Dr. Gray a lot of credit for this, we laid out what the process looked like and said how can we improve this process to make sure that it is going to work faster.

Mr. STUPAK. So if you are trying to improve the process, and my question was, what special expertise does OMB have that you don't have?

Mr. PEACOCK. You need to have one entity in the government, which is going to bring together diverse scientific views. That is OMB's responsibility. I don't know who else would do it.

Mr. STUPAK. So during this process, they have to do it three times?

Mr. PEACOCK. Well, I have to tell you, this reminds me of a project my daughter did. She was supposed to do a diagram of how you make breakfast in the morning and she did one of me making waffles, and it looked something like that, and I got to tell you, I make pretty good waffles and it seems pretty simple to me and she does eat breakfast, so you can make anything look pretty complicated depending on how much specificity you go to. I am not familiar with these diagrams.

Mr. STUPAK. This is your chart. We didn't make it up. We can't understand it.

Mr. PEACOCK. I am familiar with the process that I signed out in the memorandum which lays out the steps which Dr. Gray was referring to. This to me is a logical process and each step of the process has a certain number of days assigned to it.

Mr. STUPAK. What is this then?

Mr. PEACOCK. I have no idea. The first time I have seen that chart is today in this hearing room.

Mr. STUPAK. Your staff briefed us with this chart. They gave us these charts and tried to get us to understand your process.

Mr. PEACOCK. Well, I would just suggest the subcommittee stay with what I sent out in my memorandum, which I think is pretty clear.

Mr. STUPAK. Who do we believe in the EPA then, you or the people who——

Mr. PEACOCK. I am not saying that chart is inaccurate. I am saying I am not familiar with it.

Mr. STUPAK. So do you think OMB should be involved three times in the IRIS process?

Mr. PEACOCK. I don't see how you keep OMB out of any process where you have to bring interagency comments in.

Mr. STUPAK. Right, but three times? I can see them getting everyone together like they did in 2004, before 2004.

Mr. PEACOCK. When we do a rulemaking, for instance, they are involved twice. So once again——

Mr. STUPAK. And do you think their deliberations should be open to the public?

Mr. PEACOCK. No, I don't think. I think you have two effects if you do that. One is to chill the discussion that you need in order to get good science and good policymaking, and the second is, you confuse the public sometimes.

Mr. STUPAK. And also if no one is watching you, you can do whatever you want with the proposed science.

Mr. PEACOCK. Well, that is a cynical view and there are certainly examples where that has happened. I am not convinced that it is happening right now. I don't see the evidence for it.

Mr. STUPAK. I have no further questions. Mr. Shimkus?

Mr. SHIMKUS. I don't have any questions either, Mr. Chairman.

Mr. STUPAK. Well, thank you. Thank you for coming, and this panel is dismissed.

That concludes all questioning. I want to thank all the witnesses for coming today and for their testimony. I ask unanimous consent that the hearing record will remain open for 30 days for additional questions for the record. Without objection, the record will remain open. I ask unanimous consent that the contents of our document binder be entered into the record. Without objection, the documents will be entered the record.

That concludes our hearing, and without objection, this meeting of the subcommittee is adjourned.

[Whereupon, at 3:48 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

PREPARED STATEMENT OF HON. GENE GREEN

Thank you Mr. Chairman for holding this hearing on the integrity of EPA science, an important issue of mutual interest to our two Subcommittees.

The Subcommittee on Oversight and Investigations has done a valuable and important job this Congress is identifying and investigating issues that require legislative follow-up by our legislative Subcommittees.

As the new Chairman, I would like to assure everyone that the Subcommittee on the Environment and Hazardous Materials is following these proceedings and investigations closely.

Chairman Stupak is a persistent investigator and legislator and I know this Subcommittee will follow the trail wherever it leads.

If these investigations determine that legislative follow-up is needed to ensure the integrity of EPA science for the public, then the Environment and Hazardous Materials Subcommittee will stand ready to develop whatever legislative changes may be necessary.

Risk assessment is a critical component in the protection of public health and the environment. Without adequate risk assessment, legislators and regulators cannot make informed and wise decisions about risk management.

The testimony of John Stephenson from the Government Accountability Office is not encouraging on this point.

EPA has a responsibility to manage the Integrated Risk Information System (IRIS) to inform the public, industry, and policy-makers with the strongest and best available science on a variety of potentially hazardous materials.

I am particularly concerned that EPA has not been able to complete an IRIS assessment for dioxin, a compound that we know is very dangerous and is far to prevalent in and around my district along the Houston Ship Channel.

Just outside our district we have the San Jacinto Waste Pits Superfund site, which consists of submerged waste pits from an old paper mill that were recently discovered to be leaching high levels of dioxin out into the San Jacinto River, and from there possibly to Galveston Bay.

Fish advisories have been extended to larger and larger areas, creating a threat both to people who fish for food and for the large sport fishing industry in the area.

Dioxin's status as a toxic compound should not be controversial, so the lack of a complete its risk assessment is very discouraging. Apparently only four risk assessments have been completed this year, with a backlog of 70 more waiting behind them.

Twelve of these backlogged risk assessments have been in process for more than 9 years. EPA is taking as long to complete a risk assessment as Congress takes to rewrite the Clean Air Act.

While EPA appears to make little progress on the backlog of 70 assessments, GAO's testimony indicates that nearly half of the 540 existing assessments may be out of date.

Making matters worse, hundreds of requested assessments on additional chemicals have not yet made their way into the IRIS database.

With the recent public attention to chemicals such as Thah-Lates (pthalates), BPA, and flame retardants, it seems that our chemical regulatory system is lurching from one public flash-point to another, while systematic risk assessment and risk management are stuck in neutral.

If the wheels are just spinning over at EPA, Congress will be forced move on its own in response to a public outcry for protection from potentially hazardous chemicals.

We need to restore public confidence in EPA's risk assessment and chemical regulatory system, and the first step must be to ensure the integrity of EPA's scientific information and practices.

Mr. Chairman, thank you for holding this hearing. The Subcommittee on Environment and Hazardous Materials looks forward to working with this Subcommittee on any and all issues that you identify involving problems with EPA science.

PREPARED STATEMENT OF HON. MARSHA BLACKBURN

Mr. Chairman, thank you for holding this hearing and I want to thank the witnesses for testifying before this committee on scientific integrity at the EPA.

Some members in this committee and witnesses on these panels believe the current administration has significantly interfered with science review and policy in the EPA over the past 8 years.

Yet there is also evidence of staff and scientists within EPA either interfering or not complying with the peer review process

These actions severely undermine the credibility of EPA to objectively regulate environmental pollutants.

One recent example is EPA's reliance on NOAA's "Unified Synthesis Product" to support its proposed greenhouse gas regulations.

This document was made to look like real science. It was touted as a highly influential scientific assessment.

But in fact there was no actual research, and the scientific method was thrown to the wayside.

A proper peer review would have excluded this document from consideration.

Another example is the recent comments made at the December 2007 meeting of the Board of Scientific Counselors Computational Toxicology Subcommittee.

These comments revealed how EPA investigators are cheating on their results for suitable data and the lack of any evidentiary support for EPA's current use of linear modeling for low dose toxic claims.

Has a proper peer review been conducted on these issues? It appears not.

Mr. Chairman, scientific integrity is a commitment to truthfulness, personal accountability, and adherence to standards of professional conduct.

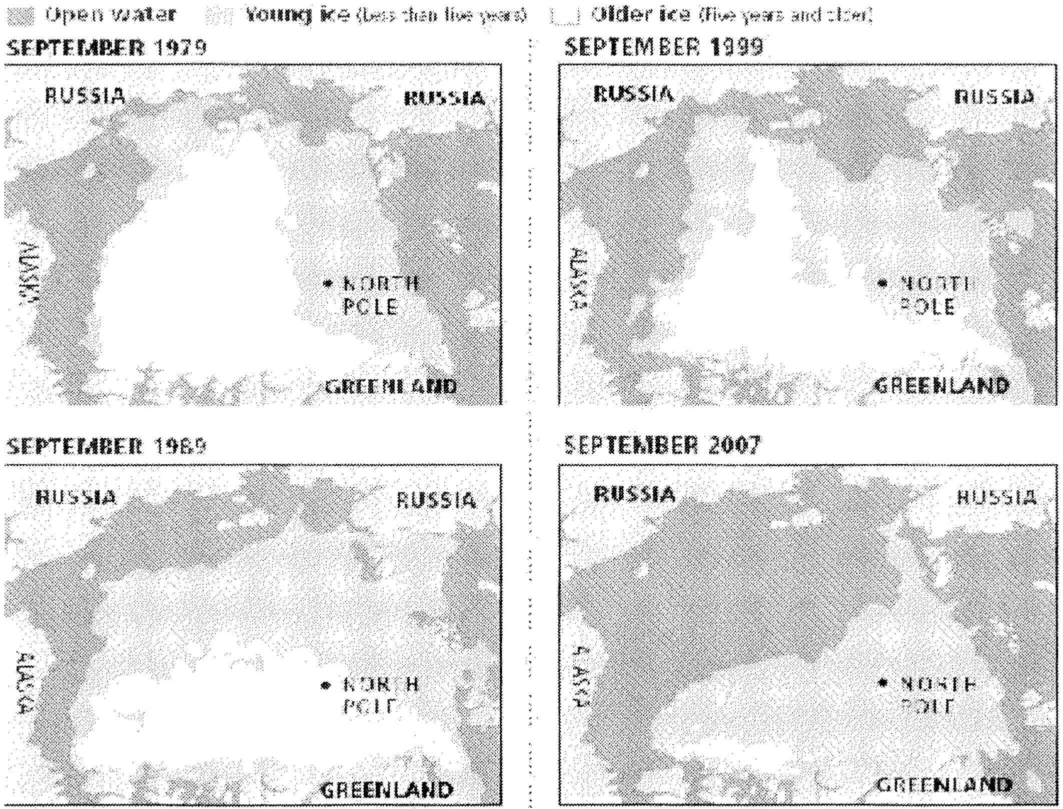
But conflicts of interest can threaten scientific integrity and improperly influence decision makers who must rely on the assessments for public policy.

And the conflicts need not be financial. They may stem from personal views or desire for more power in a position.

Or, in some cases, the conflicts can come from dependence upon a source that funds the research—industry, government, and even NGOs.

I urge my colleagues to look at the issue on a broad basis and not merely focus on one side of the equation.

I yield the balance of my time.



Sources: National Snow and Ice Data Center, Boulder, Colo.;
Ignatius Rigor, Jamie Morison, Ron Lindsay, University of Washington Applied Physics Laboratory

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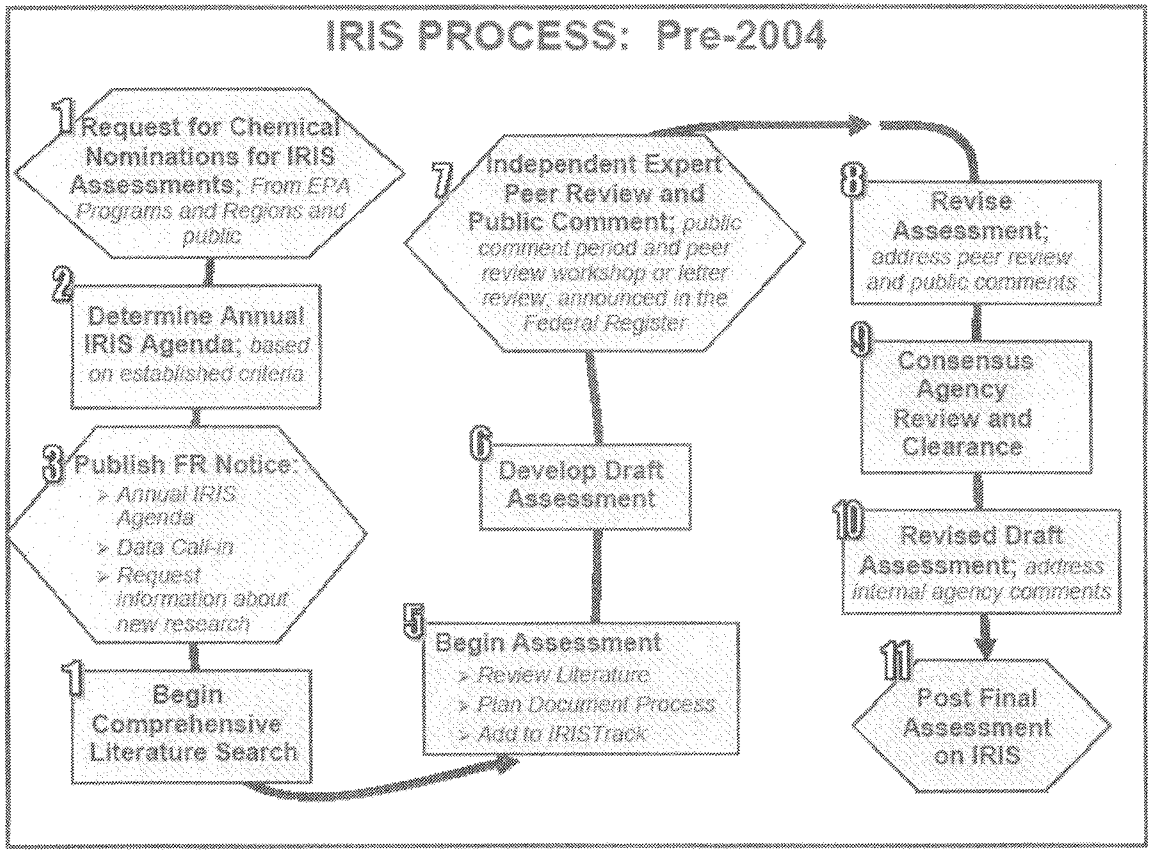


IRIS PROCESS: Pre-2004

1 **Request for Chemical Nominations for IRIS Assessments;** *From EPA Programs and Regions and public*

2 **Determine Annual IRIS Agenda;** *based on established criteria*

3 **Publish FR Notice:**
- *Annual IRIS Agenda*
- *Data Call-in*
- *Request information about new research*

1 **Begin Comprehensive Literature Search**

5 **Begin Assessment**
- *Review Literature*
- *Plan Document Process*
- *Add to IRISTrack*

6 **Develop Draft Assessment**

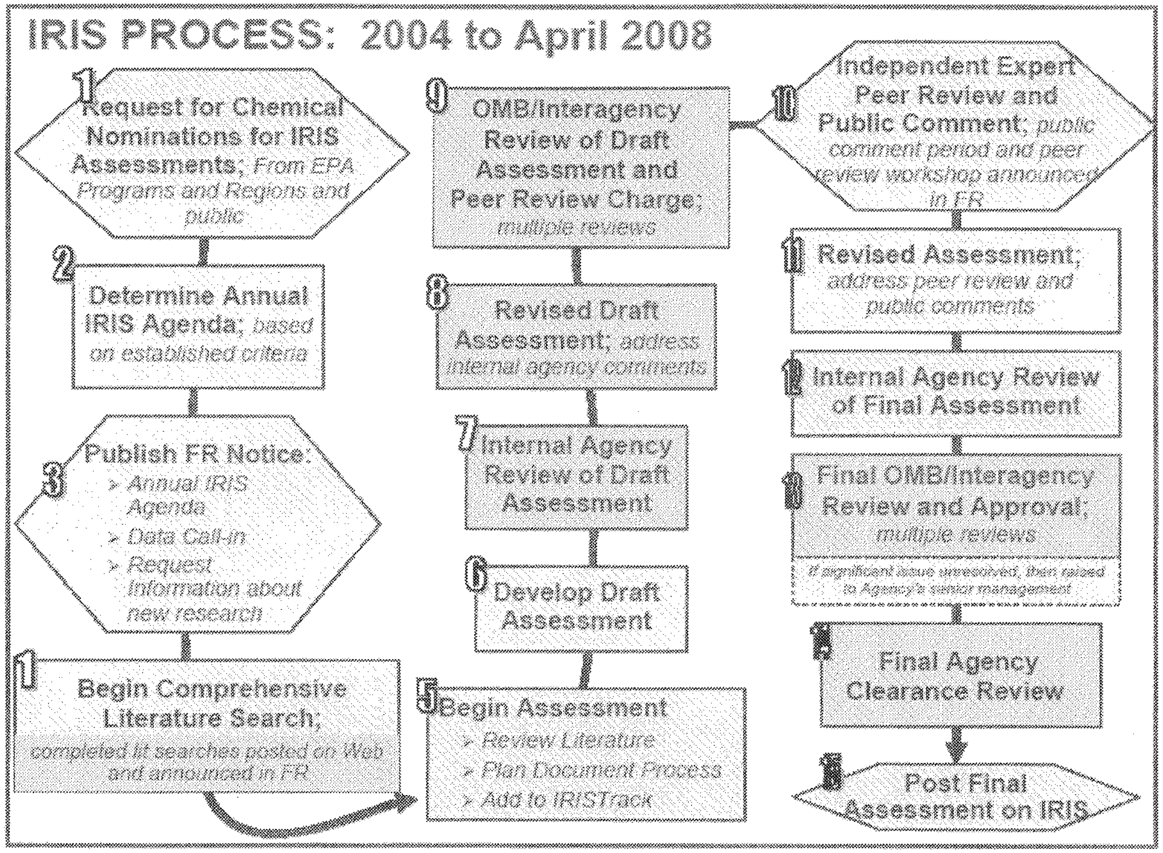
7 **Independent Expert Peer Review and Public Comment;** *public comment period and peer review workshop or letter review, announced in the Federal Register*

8 **Revise Assessment;** *address peer review and public comments*

9 **Consensus Agency Review and Clearance**

10 **Revised Draft Assessment;** *address internal agency comments*

11 **Post Final Assessment on IRIS**



IRIS PROCESS: 2004 to April 2008

1 **Request for Chemical Nominations for IRIS Assessments;** *From EPA Programs and Regions and public*

2 **Determine Annual IRIS Agenda;** *based on established criteria*

3 **Publish FR Notice:**
- *Annual IRIS Agenda*
- *Data Call-in*
- *Request Information about new research*

4 **Begin Comprehensive Literature Search;** *completed lit searches posted on Web and announced in FR*

5 **Begin Assessment**
- *Review Literature*
- *Plan Document Process*
- *Add to IRISTrack*

6 **Develop Draft Assessment**

7 **Internal Agency Review of Draft Assessment**

8 **Revised Draft Assessment;** *address internal agency comments*

9 **OMB/Interagency Review of Draft Assessment and Peer Review Charge;** *multiple reviews*

10 **Independent Expert Peer Review and Public Comment;** *public comment period and peer review workshop announced in FR*

11 **Revised Assessment;** *address peer review and public comments*

12 **Internal Agency Review of Final Assessment**

13 **Final OMB/Interagency Review and Approval;** *multiple reviews*

If significant issue unresolved, then raised to Agency's senior management

14 **Final Agency Clearance Review**

15 **Post Final Assessment on IRIS**

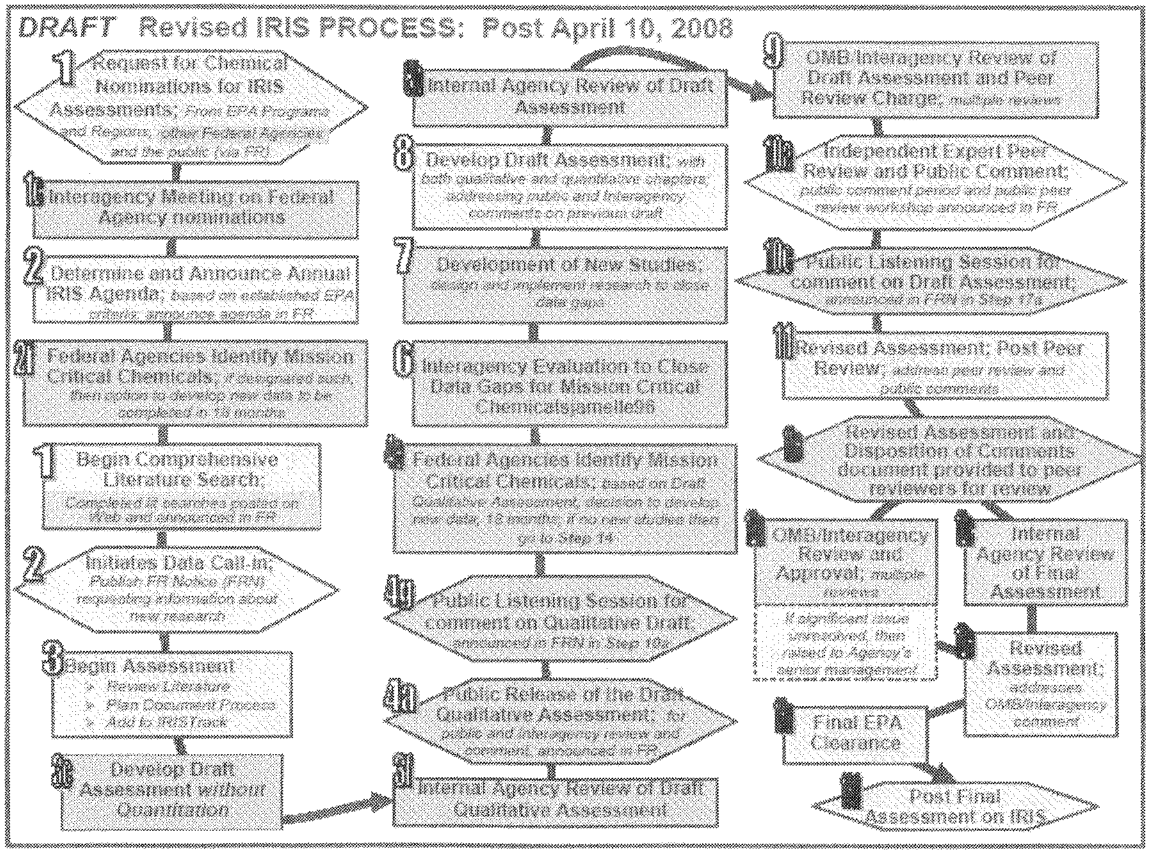
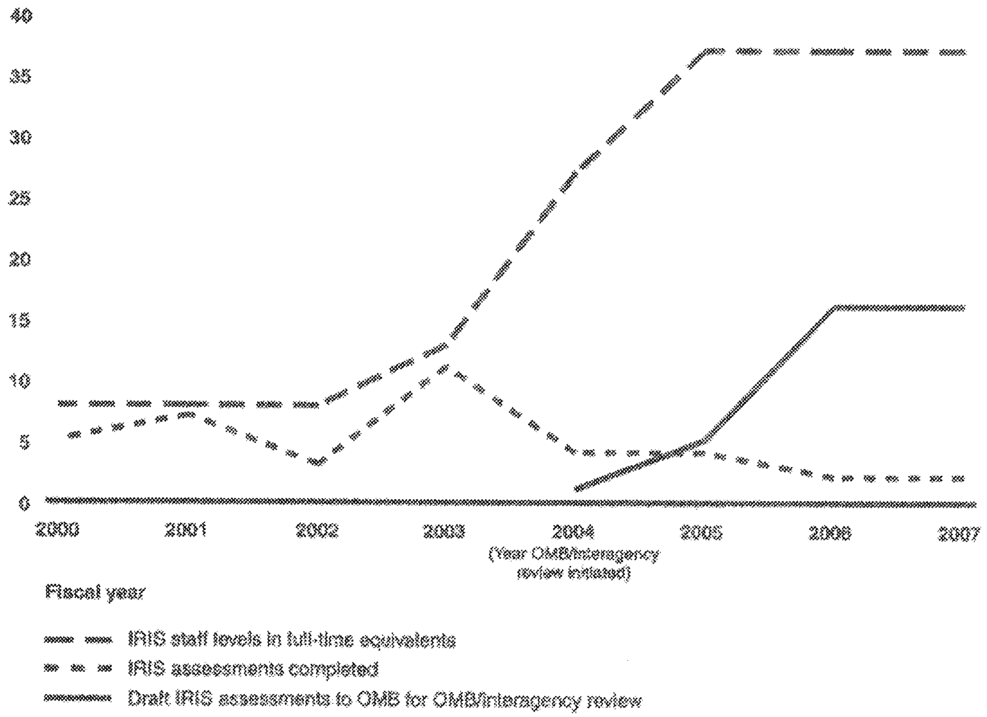
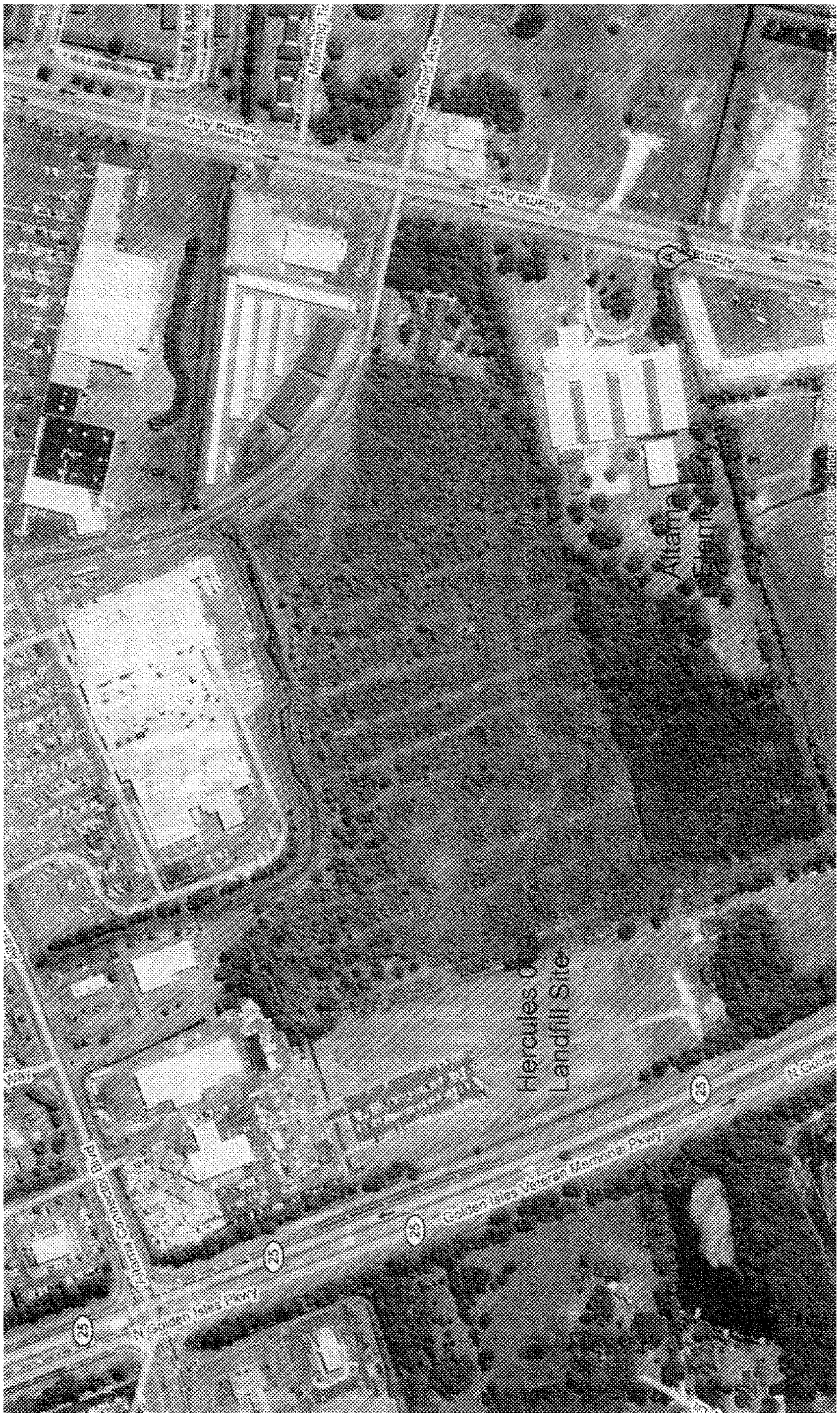

DRAFT Revised IRIS PROCESS: Post April 10, 2008
1
Request for Chemical Nominations for IRIS Assessments; From EPA Programs and Regions, other Federal Agencies and the public (via FR)
Interagency Meeting on Federal Agency nominations
2
Determine and Announce Annual IRIS Agenda; based on established EPA criteria; announce agenda in FR
Federal Agencies Identify Mission Critical Chemicals; if designated such, then option to develop new data to be completed in 18 months
1
Begin Comprehensive Literature Search; Completed lit searches posted on Web and announced in FR
2
Initiates Data Call-In; Publish FR Notice (FRN) requesting information about new research
3
Begin Assessment
Review Literature
Plan Document Process
Add to IRISTrack
Develop Draft Assessment without Quantitation
Internal Agency Review of Draft Assessment
8
Develop Draft Assessment; with both qualitative and quantitative chapters, addressing public and Interagency comments on previous draft
7
Development of New Studies; design and implement research to close data gaps
6
Interagency Evaluation to Close Data Gaps for Mission Critical Chemicalsjsmelle96
Federal Agencies Identify Mission Critical Chemicals; based on Draft Qualitative Assessment, decision to develop new data, 18 months; if no new studies then go to Step 14
Public Listening Session for comment on Qualitative Draft; announced in FRN in Step 10a
Public Release of the Draft Qualitative Assessment; for public and interagency review and comment, announced in FR
Internal Agency Review of Draft Qualitative Assessment
9
OMB/Interagency Review of Draft Assessment and Peer Review Charge; multiple reviews
Independent Expert Peer Review and Public Comment; public comment period and public peer review workshop announced in FR
Public Listening Session for comment on Draft Assessment; announced in FRN in Step 17a
11
Revised Assessment; Post Peer Review; address peer review and public comments
Revised Assessment and Disposition of Comments document provided to peer reviewers for review
OMB/Interagency Review and Approval; multiple reviews
If significant issue unresolved, then raised to Agency's senior management
Internal Agency Review of Final Assessment
Revised Assessment; addresses OMB/Interagency comment
Final EPA Clearance
Post Final Assessment on IRIS

Figure 2: Number of Completed IRIS Assessments, Draft Assessments to OMB, and IRIS Staff in Full-Time Equivalents, Fiscal Years 2000-2007



Source: GAO analysis of EPA data.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Hercules
Landfill Site
Altama
Golden Isles Veterans Memorial Pkwy
N Golden Isles Pkwy
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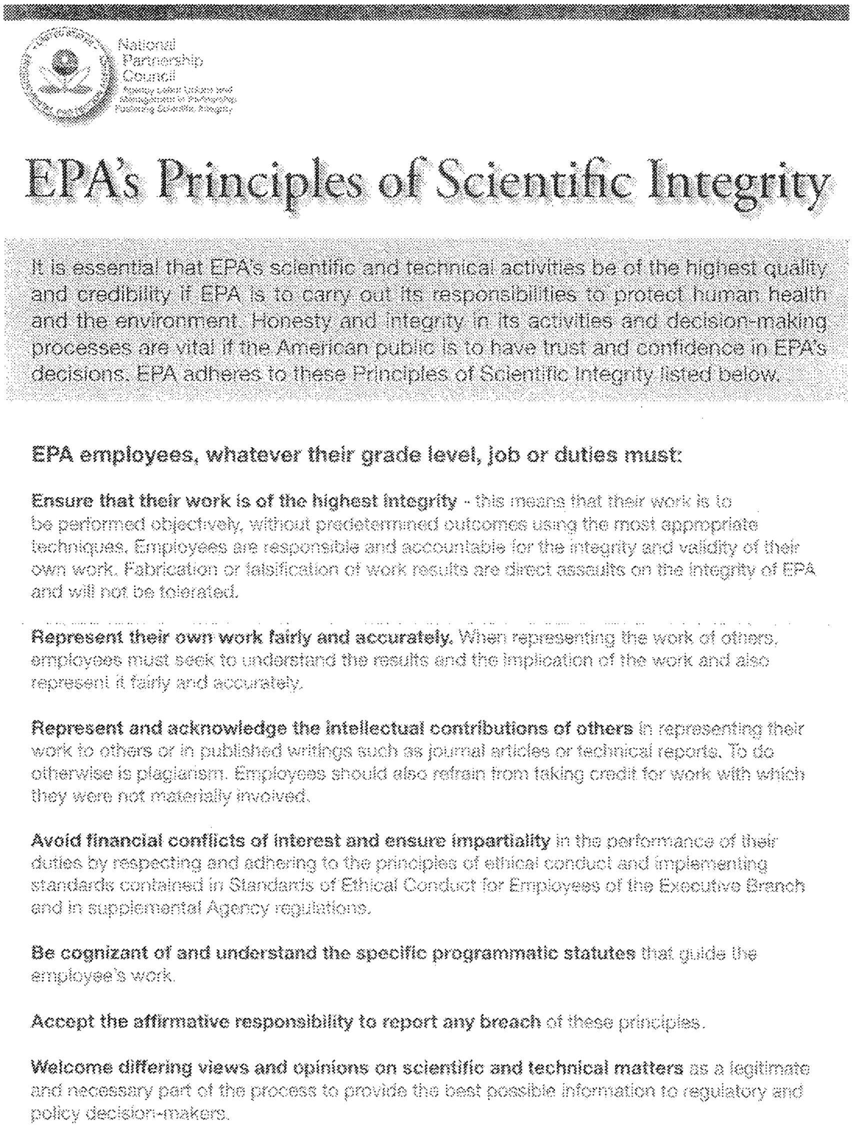
Item #	Description	Date
	Interference with Scientists	
1	EPA's Principles of Scientific Integrity	
2	Union of Concerned Scientists report, "Interference at the EPA."	April 2008
3	GAO Report (GAO-08-440), "Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System."	March 2008
	IRIS Documents	
4	IRIS Process (Pre-2004; 2004 to 2008; Post April 10, 2008)	
5	EPA internal memo from Marcus Peacock to George Gray, re: "Implementation of Revised IRIS Process."	04/10/08
	Deborah Rice related documents	
6	Letter from Sharon Kneiss, American Chemistry Council (ACC) VP, to EPA Assistant Administrator George Gray, re: "IRIS Peer Review of PBDEs..."	05/03/07
7	Letter from ACC's Nancy Sandrof to EPA's George Gray, re: "IRIS Peer Review of PBDEs..."	09/21/07
8	Letter from ACC's Nancy Sandrof to EPA's George Gray, re: "IRIS Peer Review of PBDEs..."	12/19/07
9	Letter from EPA's George Gray to ACC's Nancy Sandrof, re: September 21, 2007 letter.	01/08/08
10	Letter Maine Governor John Baldacci to EPA Administrator Stephen Johnson.	03/17/08
11	Letter from Marcus Peacock to EPA Deputy Inspector General Bill Roderick.	04/10/08
12	External Peer Review: Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs) Human Health Assessment-Final Report (with Deborah Rice).	February 2007
13	External Peer Review: Toxicological Review for PBDEs Human Health Assessment-Final Report (without Deborah Rice).	February 2007
14	External Peer Review: Toxicological Review for PBDEs Human Health Assessment-Final Report (without Deborah Rice; with Disclaimer).	February 2007
15	Toxicological Review of Decabromodiphenyl Ether (with Deborah Rice, chair).	June 2008
	Toxaphene Documents	
16	EPA Inspector General Ombudsman Report: "Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia (Report 2005-P-00022)."	09/26/05

17	EPA Memo from Paul McKechnie to J. I. Palmer, Jr., subject: "OIG Ombusman Report 2005-P-00022."	10/31/06
18	EPA Inspector General Ombudsman Report, "More information is Needed on Toxaphene Degradation Products (Report 2006-P-00007)."	12/16/05
19	EPA Memo from Marcus Peacock to Bill Roderick, subject: "Response to Ombudsman Report 2006-P-00007."	08/30/06
20	HHS Agency for Toxic Substances & Disease Registry Public Health Assessment, "Terry Creek Dredge Spoil Areas/Hercules Outfall Site, Brunswick, Glynn County, Georgia."	
21	U S. Army Corps of Engineers Five-Year Review Report (Second Five-Year Report) for Hercules 009 Landfill.	February 2004
22	Letter from Georgia Department of Natural Resources Hazardous Waste Management Program Manager Jim Ussery to Leo Francendese (EPA Region IV), re: Second Five-Year Report on Hercules 009 Landfill.	06/04/04
23	Letter from Hercules Lanfill to Leo Francendese, re:Second Five-Year Report.	05/07/04
24	Federal Register: Environmental Protection Agency: Drinking Water Contaminant Candidate	02/21/08
25	The Weinberg Group document: "Toxaphene Risk Assessment: Re-evaluation and Data Development."	08/21/07
26	Regulatory Toxicology and Pharmacology (journal) article by Ted Simon, et al. "Development of a Reference Dose for the Persistent Congeners of Weathered Toxaphene Based on in vivo and in vitro Effects Related to Tumor Promotion."	09/26/05
27	International Journal of Occupational and Environmental Health Special Contribution, "Correspondence about Publication Ethics and Regulatory Toxicology and Pharmacology."	11/19/02



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EPA's Principles of Scientific Integrity

It is essential that EPA's scientific and technical activities be of the highest quality and credibility if EPA is to carry out its responsibilities to protect human health and the environment. Honesty and integrity in its activities and decision-making processes are vital if the American public is to have trust and confidence in EPA's decisions. EPA adheres to these Principles of Scientific Integrity listed below.

EPA employees, whatever their grade level, job or duties must:

Ensure that their work is of the highest integrity - this means that their work is to be performed objectively, without predetermined outcomes using the most appropriate techniques. Employees are responsible and accountable for the integrity and validity of their own work. Fabrication or falsification of work results are direct assaults on the integrity of EPA and will not be tolerated.

Represent their own work fairly and accurately. When representing the work of others, employees must seek to understand the results and the implication of the work and also represent it fairly and accurately.

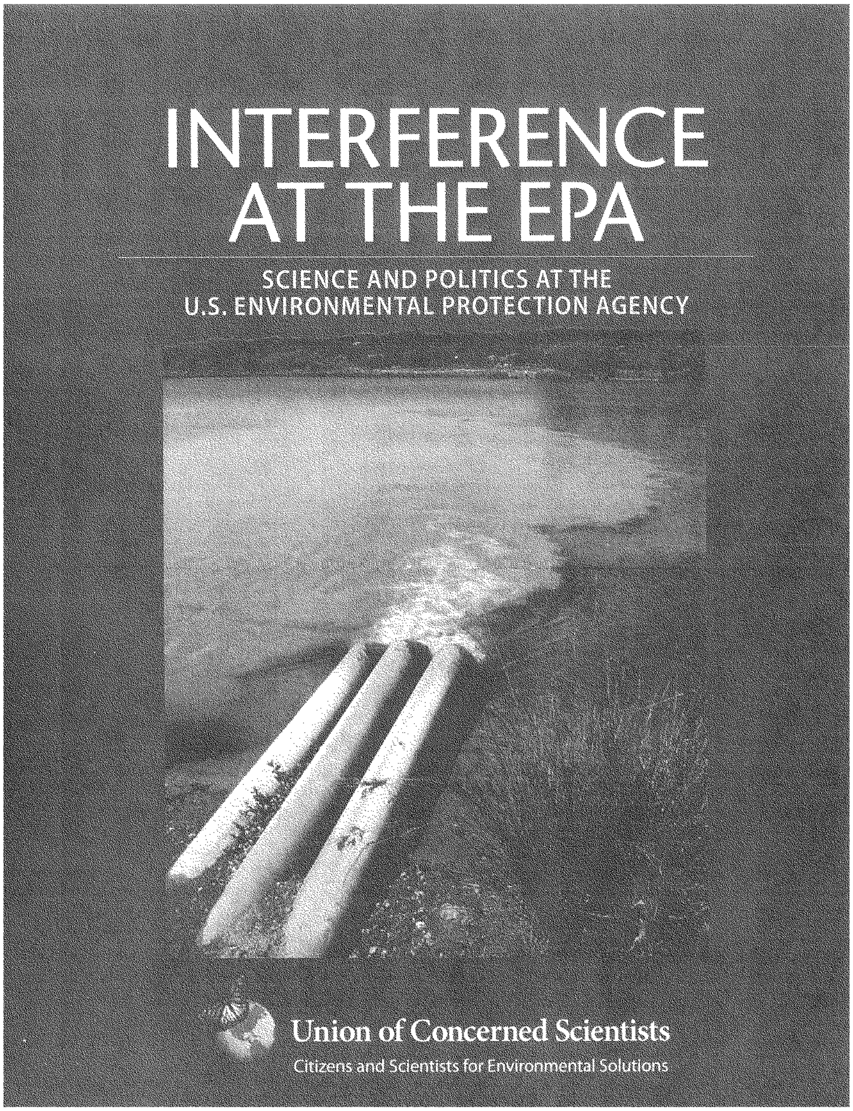
Represent and acknowledge the intellectual contributions of others in representing their work to others or in published writings such as journal articles or technical reports. To do otherwise is plagiarism. Employees should also refrain from taking credit for work with which they were not materially involved.

Avoid financial conflicts of interest and ensure impartiality in the performance of their duties by respecting and adhering to the principles of ethical conduct and implementing standards contained in Standards of Ethical Conduct for Employees of the Executive Branch and in supplemental Agency regulations.

Be cognizant of and understand the specific programmatic statutes that guide the employee's work.

Accept the affirmative responsibility to report any breach of these principles.

Welcome differing views and opinions on scientific and technical matters as a legitimate and necessary part of the process to provide the best possible information to regulatory and policy decision-makers.



INTERFERENCE AT THE EPA

SCIENCE AND POLITICS AT THE U.S. ENVIRONMENTAL PROTECTION AGENCY

Union of Concerned Scientists

Citizens and Scientists for Environmental Solutions

INTERFERENCE AT THE EPA

SCIENCE AND POLITICS AT THE U.S. ENVIRONMENTAL PROTECTION AGENCY

The Scientific Integrity Program of the
Union of Concerned Scientists

APRIL 2008

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The Union of Concerned Scientists is the leading science-based nonprofit working for a healthy environment and a safer world.

The UCS Scientific Integrity Program mobilizes scientists and citizens alike to defend science from political interference and restore scientific integrity to policy making. More information about UCS and the Scientific Integrity Program is available online at *www.ucsusa.org/scientific_integrity*.

The full text of this report is available on the UCS website (*www.ucsusa.org/publications*) or may be obtained from:

UCS Publications
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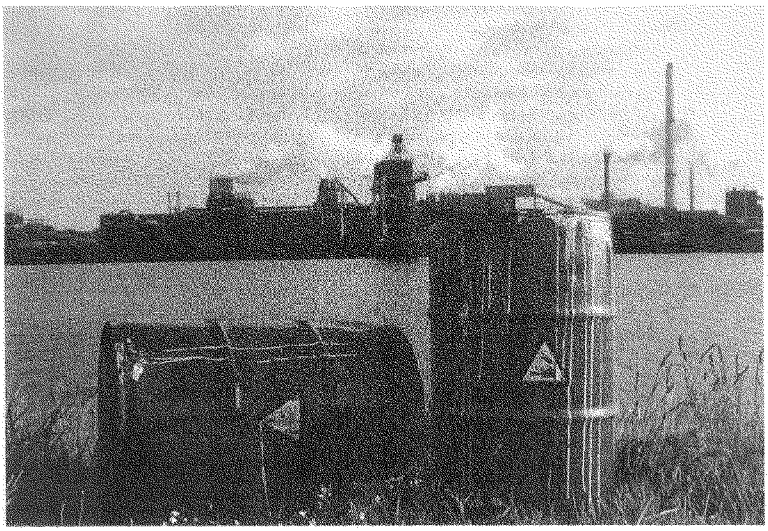
Executive Summary

The U.S. Environmental Protection Agency (EPA) has the simple yet profound charge "to protect human health and the environment." EPA scientists apply their expertise to protect the public from air and water pollution, clean up hazardous waste, and study emerging threats such as global warming. Because each year brings new and potentially toxic chemicals into our homes and workplaces, because air pollution still threatens our public health, and because environmental challenges are becoming more complex and global, a strong and capable EPA is more important than ever.

Yet challenges from industry lobbyists and some political leaders to the agency's decisions have too often led to the suppression and distortion of the scientific findings underlying those decisions—to the detriment of both science and the health of our nation. While every regulatory agency must balance scientific findings with other considerations, policy makers need access to the highest-quality scientific information to make fully informed decisions.

Concern over this problem led the Union of Concerned Scientists (UCS) to investigate political interference in science at the EPA. In the summer of 2007, UCS, working with the Center for Survey Statistics and Methodology at Iowa State University, distributed a 44-question survey to nearly 5,500 EPA scientists, asking for information about political interference in their scientific



work, the use of science in EPA decision making, barriers to communication, employee morale, and the agency's effectiveness. UCS identified these scientists through EPA websites, consultations with current and former employees, and targeted Internet searches.

> **There are still good scientists producing good science at USEPA. The main problem I see is an administration that considers science only if it supports its agenda. As in other areas, science is used only if it furthers preexisting policy; otherwise it is ignored, marginalized or suppressed (e.g. climate change).**
>
> A scientist from the EPA regional offices

We received completed surveys from 1,586 scientists, for a response rate of 29 percent. These respondents represented every scientific program office at EPA headquarters, all 10 regional offices, and more than a dozen research laboratories across the country. Most respondents were agency veterans, with more than a decade of experience at the EPA. Beyond specific survey questions, more than 850 scientists also provided written comments in response to an open-ended essay question. To add to this information, UCS interviewed dozens of current and former EPA scientists.

The results of these investigations show an agency under siege from political pressures. On numerous issues—ranging from mercury pollution to groundwater contamination to climate change—political appointees of the George W. Bush administration have edited scientific documents, manipulated scientific assessments, and generally sought to undermine the science behind dozens of EPA regulations.

These findings highlight the need for strong reforms to protect EPA scientists, make agency decision making more transparent, and reduce politicization of the regulatory process.

Political Interference in Scientific Work

Large numbers of EPA scientists reported widespread and inappropriate interference by EPA political appointees, the White House, and other federal agencies in their scientific work:

- 889 scientists (60 percent of respondents*) personally experienced at least one incident of political interference during the past five years.
- Among EPA veterans (scientists with more than 10 years of experience at the agency), 409 (43 percent) said interference occurred more often in the past five years than in the previous five-year period.

EPA scientists also reported personally experiencing specific forms of political interference, from the explicit to the subtle:

- 94 scientists (7 percent) had frequently or occasionally been "directed to inappropriately exclude or alter technical information from an EPA scientific document."
- 191 scientists (16 percent) had personally experienced frequent or occasional "situations in which scientists have actively objected to, resigned from, or removed themselves from a project because of pressure to change scientific findings."
- 232 scientists (18 percent) had personally experienced frequent or occasional "changes or edits during review that change the meaning of scientific findings."
- 285 scientists (22 percent) had personally experienced frequent or occasional "selective or incomplete use of data to justify a specific regulatory outcome."

---

* Unless otherwise stated, percentages reflect the share of respondents who answered a specific question.

- 153 scientists (13 percent) had personally experienced frequent or occasional "pressure to ignore impacts of a regulation on sensitive populations."

- 299 scientists (24 percent) had personally experienced frequent or occasional "disappearance or unusual delay in the release of websites, press releases, reports, or other science-based materials."

- 394 scientists (31 percent) had personally experienced frequent or occasional "statements by EPA officials that misrepresent scientists' findings."

Respondents indicated that political interference arose from both internal and external sources:

- 516 scientists (43 percent) knew of "many or some" cases where EPA political appointees had inappropriately involved themselves in ~~scientific decisions~~.

- 560 scientists (49 percent) knew of "many or some" cases where political appointees at other federal agencies had inappropriately involved themselves in decisions.

- 507 scientists (42 percent) knew of "many or some" cases where "commercial interests have inappropriately induced the reversal or withdrawal of EPA scientific conclusions or decisions through political intervention."

- 329 scientists (28 percent) knew of such interference by "nongovernmental or advocacy groups."

In essay responses, nearly 100 scientists identified the White House Office of Management and Budget (OMB), which oversees the federal budget and coordinates all federal regulations, as the primary source of external interference.

Respondents reported widespread respect for their direct supervisors, but had fewer commendations for the EPA's senior leaders:

- 1,282 scientists (81 percent) respected the integrity and professionalism of their direct manager or supervisor, while 686 (43 percent) said the same about the EPA's senior leaders.

- A majority of respondents (906 scientists, or 59 percent) agreed that their direct supervisor stands behind scientific staff who express politically controversial opinions.

A landfill near the Wasatch Mountains in Utah.

Rates of political interference varied widely among offices and divisions within the agency:

- The percentage of scientists reporting interference was highest in the program offices with regulatory duties, and at EPA headquarters. A total of 337 scientists in the program offices (68 percent), and 379 scientists at headquarters (69 percent), reported at least one incident of interference in the past five years.
- The percentage of scientists reporting interference was lower—although still significant—in the Office of Research and Development (ORD), the EPA's main research arm. The ORD's National Health and Environmental Effects Research Laboratory was notably freer of interference (39 percent) than any other EPA division, while its National Center for Environmental Assessment had the highest percentage of scientists reporting interference of all EPA divisions (84 percent).
- The percentages of scientists reporting interference in the 10 regional offices varied widely, from 44 percent (region 6) to 73 percent (region 9).

To place these results in context, we cite specific incidents of interference. For example, political appointees at the White House and in top positions at the EPA manipulated scientific findings and analyses regarding mercury pollution and climate change. These incidents involved pressure to change scientific methods and findings, direct editing of scientific documents by non-scientists, and delayed release of scientific reports.

A third case—involving interagency review of the EPA's assessment of toxic chemicals—illustrates the growing ability of the OMB and other federal agencies to review and second-guess the work of the EPA's scientific experts.

Barriers to the Free Communication of Science

The free communication of scientific results is a critical part of the scientific process.

Despite statements by EPA leaders asserting that the agency supports scientific openness, many scientists report that it restricts free communication of the results of taxpayer-funded research:

- 783 scientists (51 percent) disagreed or strongly disagreed that EPA policies allow scientists to "speak freely to the news media about their findings." Another 556 scientists (36 percent) had no opinion or were unsure. Only 197 scientists (13 percent) agreed that the EPA allows scientists to communicate freely with the media.

- 291 scientists (24 percent) disagreed or strongly disagreed that they are "allowed to publish work in peer-reviewed scientific journals regardless of whether it adheres to agency policies or positions."

Beyond these restrictive policies, hundreds of scientists said they fear retaliation for speaking candidly about the EPA's work. More scientists feared retaliation for speaking candidly inside the agency than outside it:

- 492 scientists (31 percent) disagreed or strongly disagreed that they could openly express concerns about the EPA's work *inside* the agency without fear of retaliation.

- 382 scientists (24 percent) disagreed or strongly disagreed that they could openly express concerns about the EPA's work *outside* the agency without fear of retaliation.

Interviews with current and former EPA scientists revealed new examples of problems in communicating scientific research. In two cases, EPA scientists were barred from presenting research on climate change at scientific conferences. Other scientists reported difficulties speaking with the media and obtaining EPA clearance to publish their findings in scientific journals.

Political interference in scientific work combined with barriers to the free communication of scientific findings affect the amount and quality of information the U.S. public receives.

> **EPA needs dynamic, scientific leadership interested in the well being of the environment and public health. EPA should not be the political agency it has become, the right hand of industry and short economic gain.**
>
> A scientist from the Office of Solid Waste
> and Emergency Response

Undermining the Role of Science in EPA Decision Making

Scientific information is the lifeblood of much of the EPA's work and the credibility of its decisions depends on the quality of its scientific work.

A plurality of EPA scientists reported that the agency's regulatory policies are consistent with its scientific findings. However, a similar number felt that the EPA could do a better job of using the best judgment of its scientific staff:

- 745 scientists (48 percent) felt that the EPA's determinations and actions are frequently or always consistent with the scientific findings in agency documents and reports.

- 719 scientists (47 percent) felt that the EPA's determinations occasionally, seldom, or never make use of the best judgment of its scientific staff.

Hundreds of EPA scientists also felt that the agency only occasionally incorporates expert advice from advisory committees into policy decisions:

- 553 scientists (36 percent) felt that the agency occasionally, seldom, or never heeds advice from independent scientific advisory committees.

Recent changes in the EPA's process for setting the National Ambient Air Quality Standards provide one prominent example of how political considerations have trumped scientific expertise and sidelined the EPA's scientific advisory committees.

> **Do not trust the Environmental Protection Agency to protect your environment. Ask questions. Be aware of political and economic motives. Become politically active. Elect officials with motives to protect the environment and hold them accountable.**
>
> A scientist from an EPA regional office

Challenges to Agency Effectiveness

Beyond political interference in EPA science, several survey questions asked respondents about other factors that could impair their ability to do their jobs, and the ability of the agency as a whole to fulfill its mission.

Large numbers of EPA scientists indicated that a lack of sufficient or appropriate resources was a serious issue in their office or division:

- 969 scientists (62 percent) disagreed or strongly disagreed that the "EPA division where I work has sufficient resources to adequately perform its mission of protecting human health and the environment."

- 555 scientists (36 percent) agreed or strongly agreed that the "recent changes and closures in the EPA library system have impaired my ability to do my job." This opinion was especially prevalent among scientists in regions 5, 6, and 7, which had their libraries closed (86 of these scientists, or 48 percent, agreed).

- 574 scientists (41 percent) agreed or strongly agreed that "the trend toward contracting out scientific work is harming the effectiveness of my division."

Survey questions also asked scientists about their job satisfaction, and the morale in their division:

- Twice as many respondents reported a decrease in job satisfaction over the past five years as those who reported an increase (670 versus 328 scientists).

- Opinions about workforce morale varied widely. A total of 564 scientists (37 percent) said morale was fair, and 387 (25 percent) said morale was poor or extremely poor. A total of 570 scientists (37 percent) said ~~morale was good or excellent~~.

Questions about the overall effectiveness of the EPA elicited a range of responses:

- Respondents were more likely to agree than disagree that the EPA was acting effectively to clean up environmental problems. A total of 812 scientists (52 percent) agreed that the EPA acts effectively to "clean up and/or mitigate existing pollution or environmental problems," while 522 (33 percent) disagreed.

- 694 scientists (44 percent) agreed that the EPA acts effectively to "foster practices that prevent environmental degradation or adverse health effects before they occur," while 629 scientists (40 percent) disagreed.

- Twice as many respondents reported a decrease in the effectiveness of their office or division over the past five years (696 scientists, or 45 percent) as those who reported an increase (321 scientists, or 21 percent).

Multiple sources of air and water pollution along a stretch of the Hudson River in Glens Falls, NY.

- Respondents were evenly split on whether the EPA is moving in the right direction. A total of 685 scientists (44 percent) disagreed that the EPA is moving in the right direction, while 624 scientists (40 percent) agreed.

Recommendations

The many forms of political interference in EPA science revealed through our survey, our interviews, and other sources of information require a suite of solutions in five major arenas: protecting EPA scientists, increasing agency transparency, reforming its regulatory process, strengthening its scientific advisory system, and depoliticizing funding, monitoring, and enforcement.

- **Protecting EPA Scientists:** The agency's scientists have a profound responsibility to the U.S. public. To fulfill that responsibility, they need reassurance that standing behind their scientific work will not open them to official or unofficial retaliation. Congress is considering several bills that would strengthen the federal whistle-blower system. Congress should pass the strongest possible protections, and the next EPA administrator should formally incorporate them into the agency's policies.

- **Making the EPA More Transparent:** Decisions made behind closed doors threaten the integrity of EPA science and the agency's ability to protect public health and the environment. Opening up these decisions to congressional and public scrutiny is an important step in revealing and ending the misuse of science.

  The EPA should institute a transparency policy for all meetings with representatives of other federal agencies and outside entities. The agency should also create procedures that ensure the periodic release of scientific documents and prevent them from remaining in draft form indefinitely. The EPA should publish a summary statement discussing the scientific basis for each significant regulatory decision, and document dissenting opinions. The agency should also reform its policies to allow scientists to communicate freely with the media, and to quickly clear their findings for publication in scientific journals, to ensure the free flow of scientific information.

- **Reforming the Regulatory Process:** The EPA was created to implement and enforce the nation's environmental laws, and it has developed the expertise, experience, processes, and policies needed to fulfill that charge. While the White House is responsible for overseeing federal agencies, it must strike a better balance between administration priorities and agency independence. The White House should respect the agency's reservoir of scientific and technical knowledge and restrain the OMB from reviewing the EPA's scientific and technical documents.

To ensure the central role of the environment in high-level decision making, the next president should elevate the EPA to a cabinet-level agency. Congress should also consider how to reform and strengthen our nation's regulatory structure, to meet the pressing environmental challenges of the twenty-first century.

- **Ensuring Robust Scientific Input to the EPA's Decision Making:** The EPA should review and strengthen how it uses the scientific expertise of its staff and external advisory committees to create policies—especially when scientific input is critical or required by law. Specifically, the next EPA administrator should work with the Clean Air Science Advisory Committee to improve the process for setting the National Ambient Air Quality Standards, to ensure that the administrator relies on the "best available science." The agency should also tighten its conflict-of-interest restrictions.
- **Depoliticizing Funding, Monitoring, and Enforcement:** Problems with funding, monitoring and enforcement also need to be addressed by Congress and the next president to ensure that the EPA is the robust environmental agency that our country needs. Congress should provide the EPA with resources commensurate with its growing responsibilities and should work to ensure that selective internal budget cuts are not used to punish inconvenient programs or offices. The next president should commit to strong and consistent enforcement of the nation's environmental laws.

Concluding Thoughts

The EPA's scientific enterprise is our nation's first line of defense against threats to public health and the environment. These threats are growing more complex and global, with the potential to harm the nation's health and prosperity. Despite notable successes, air and water pollution remain serious public health problems. Each year brings new and untested chemicals into our homes, schools, and workplaces. Climate change alone is projected to have profound impacts on public health, agriculture, the economy, and even national security.

These problems are not insurmountable. The environmental and public health successes of the past several decades show that the country can rise to the challenge of environmental threats—but only if the EPA has the proper tools. Given the complexity of today's environmental challenges, a credible scientific knowledge base is essential to an effective response. To foster and sustain a healthy scientific enterprise, Congress and the next president should take concrete steps to protect the EPA's scientists, make the agency more transparent, reform the regulatory process, strengthen the scientific advisory system, and depoliticize funding, monitoring, and enforcement.

Science is not the only element of effective policy making. However, because science enjoys widespread respect, appointed officials will always be tempted to manipulate or suppress scientific findings to support predetermined policies. Such manipulation is not only dishonest; it undermines the EPA's credibility and affects the health and safety of Americans.

The Bush administration's direct abuse of science—combined with systemic changes to the regulatory system that threaten the integrity of EPA science—highlight the need for strong action by the next president and Congress to restore scientific integrity to the agency's decision making. Only then can the EPA fully mobilize to serve the public good and ensure the nation's health.

CHAPTER 1
Introduction

Christine Todd Whitman, a former Republican governor of New Jersey who was George W. Bush's first administrator of the U.S. Environmental Protection Agency (EPA), resigned her post in the summer of 2003. In a later interview, she revealed that her departure came as a direct response to the White House's weakening of EPA regulations on air pollution from aging power plants. According to Whitman, Vice President Dick Cheney pushed hard for a rule that "didn't hamper industry," and the final rule was written "at the direction of the White House," over the objections of Whitman and EPA staff. Whitman resigned rather than having to publicly defend the new rule, attesting that, "I just couldn't sign it. The president has a right to have an administrator who could defend it, and I just couldn't" (Becker and Gellman 2007).

EPA decisions have often proved controversial. However, Whitman's experience illustrates how thoroughly the EPA has become politicized under the George W. Bush administration, and how top executive branch officials have overruled the best advice of the agency's experts, at times illegally. Under this administration, political appointees have rewritten scientific documents about climate change, pressured EPA scientists to support pre-determined conclusions about mercury pollution, and sidelined the advice of the EPA's independent advisory committees in setting air pollution standards. In these and other examples, political appointees used tainted science to justify weaker protections of public health and the environment.

In contrast, Russell Train, who served as EPA administrator under Presidents Nixon and Ford, attested that, "In all my time at the EPA, I don't recall any regulatory decision that was driven by political considerations. More to the present point, never once, to my best recollection, did either the Nixon or Ford White House ever try to tell me how to make a decision" (Train 2003).

Christine Todd Whitman served as EPA administrator under President George W. Bush until her resignation in 2003 over White House interference in EPA air pollution regulations.

Political interference in EPA science threatens the health and safety of Americans. EPA scientists apply their expertise to protect the public from air and water pollution, to clean up hazardous waste, and to study emerging threats such as climate change. Because each year brings new, potentially toxic chemicals into our homes and workplaces, because air pollution still threatens our health, and because environmental challenges are growing more complex and global, a strong and capable EPA is more important than ever. Without access to the best scientific information, policy makers cannot make fully informed decisions. And without safeguards to ensure the independence of its scientific work, the EPA cannot fulfill its mission.

The past seven years have seen an epidemic of interference in the work of federal science and regulatory agencies (UCS 2008). The science underlying federal decisions has become a favored battlefield for weakening, delaying, and reversing government regulation. To assess the extent of abuses of science and allow federal scientists to tell their own stories, the Union of Concerned Scientists (UCS) has conducted a series of surveys of government scientists. Past surveys have given voice to more than 1,800 scientists working at nine federal agencies.*

> **In all my time at the EPA, I don't recall any regulatory decision that was driven by political considerations. More to the present point, never once, to my best recollection, did either the Nixon or Ford White House ever try to tell me how to make a decision.**
>
> Russell Train, EPA administrator under Presidents Nixon and Ford

To explore politicization of science at the EPA, UCS distributed a 44-question survey to nearly 5,500 EPA scientists in the summer of 2007, asking for information about how the agency uses science in its decision making. More than 1,500 scientists responded. Their answers show an agency under siege. Hundreds of EPA scientists report political interference in their work, significant barriers to the free communication of scientific results, and concerns about the agency's effectiveness. This report details these findings. It also outlines cases of political interference in the EPA's scientific work that we obtained through interviews with current and former EPA employees, Freedom of Information Act requests, and earlier UCS and media reports.

To provide context for our findings, Chapter 2 briefly summarizes the history of the EPA, outlines the key laws giving the agency its mandate, highlights its scientific program offices, and shows funding trends for the agency. Chapter 3 explains how we conducted our survey and investigation. Chapters 4, 5, 6, and 7 present our findings in four major areas: political interference in EPA science, barriers to free communication of the agency's scientific findings, the undermining of science in agency decision making, and other challenges to the agency's effectiveness. Chapter 8 presents our recommendations for restoring scientific integrity to EPA decision making, and for strengthening the agency's ability to fulfill its mission.

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* These surveys have included scientists at the U.S. Fish and Wildlife Service (UCS and PEER 2005a), the National Oceanic and Atmospheric Administration Fisheries Service (UCS and PEER 2005b), the U.S. Food and Drug Administration (UCS and PEER 2006), and climate change scientists working at seven federal agencies and the independent National Center for Atmospheric Research (UCS and GAP 2007). For survey results and essay responses, see *www.ucsusa.org/surveys.*

CHAPTER 2

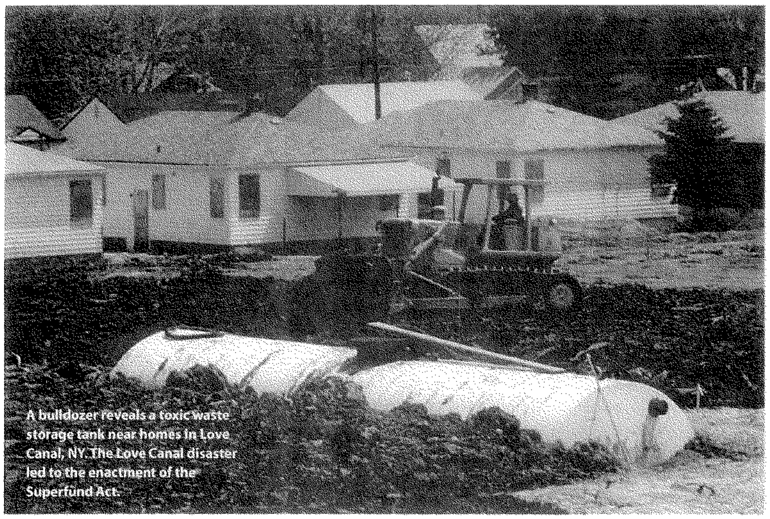
History and Organization of the EPA

The U.S. Environmental Protection Agency is charged with a simple yet profound mission: "to protect human health and the environment." To carry out this mission, the EPA implements and enforces the nation's environmental laws, monitors major environmental indicators, serves as a clearinghouse for environmental information, and conducts basic and applied research.

History

The EPA was created in 1970, a year that saw a national groundswell of environmental activism. On New Year's Day 1970, President Richard M. Nixon signed the National Environmental Policy Act. On April 22, the first Earth Day sparked actions and celebrations by millions of Americans across the nation. President Nixon also formed the Council on Environmental Quality under the leadership of Russell Train, and announced the formation of an independent federal agency to oversee the nation's environmental policy. Congress approved this plan, and the EPA opened its doors on December 2, 1970, led by Administrator William D. Ruckelshaus.

The EPA achieved many notable successes in its early years, such as a ban on the domestic use of the pesticide DDT, the phaseout of leaded gasoline, and national standards for air and water quality. Groundbreaking legislation passed by Congress in the 1970s and early 1980s made these successes possible. Building on this broad legislative mandate, the EPA has grown in scope and responsibility, with its authority now encompassing air pollution, the safety of our drinking



A bulldozer reveals a toxic waste storage tank near homes in Love Canal, NY. The Love Canal disaster led to the enactment of the Superfund Act.

water, cleanup of our toxic waste legacy, and basic scientific research into emerging environmental issues such as endocrine-disrupting chemicals and global climate change.

> **The EPA has no natural constituency. It is a job where the administrator antagonizes the oil industry one week, the auto industry the next, the farmers the next. Your hope is you don't antagonize more than one the same week.**
>
> William Reilly, EPA administrator for the first President Bush

However, with these successes has come opposition to environmental regulation from sectors of the business community and certain political interests. EPA regulations touch upon almost all aspects of the economy, often bringing the agency into conflict with industries and state and local governments. As William Reilly, EPA administrator for the first President Bush, put it: "The EPA has no natural constituency. It is a job where the administrator antagonizes the oil industry one week, the auto industry the next, the farmers the next. Your hope is you don't antagonize more than one the same week" (Coile 2003).

President Ronald Reagan considered many environmental regulations excessively harmful to the economy, and campaigned on a promise to reduce regulation and the size of the federal government. Reagan's first EPA administrator, Anne Gorsuch, attempted to weaken or reverse many EPA regulations. Gorsuch was later held in contempt of Congress for refusing to release documents relating to mismanagement of the Superfund program, and resigned amid widespread scandal. To right the ship, Reagan brought back the widely respected Ruckleshaus to succeed Gorsuch as interim administrator.

Continued political and industry opposition to environmental regulation has prompted the EPA to pursue other tactics beyond pure regulation to achieve its goals. These tactics have included a greater focus on pollution prevention and voluntary programs, as well as market-based approaches such as systems for trading pollution credits. (For a more detailed look at EPA history, see EPA 2008e.) Despite these efforts, the history of antagonism to environmental regulation from some interests, noted by Administrator Reilly, laid the groundwork for the current Bush administration's political interference in the EPA's scientific work.

Key Environmental Laws

The EPA website lists more than 30 federal laws that provide authorization for the EPA's activities (EPA 2008b; see also Lee 2001, a report from the Congressional Research Service). Congress has amended and updated many of these laws in the intervening years. About a dozen are the most important:

- The **National Environmental Policy Act of 1969** (NEPA) established the Council on Environmental Quality and led to the founding of the EPA. NEPA declares a "national policy to encourage productive and enjoyable harmony between man and his environment," and requires federal agencies to consider the environmental results before undertaking any significant action, through a publicly available environmental impact statement (EIS). The EPA is responsible for reviewing, commenting on, and archiving EISs from other federal agencies.

- The **Clean Air Act** (CAA, 1970) establishes a range of standards and procedures for controlling air pollution. Under the act, the EPA is responsible for setting national standards for six "criteria" air pollutants (those that affect ambient air quality, such as ozone, particulate matter, and lead), 188 specific hazardous air pollutants, and the pollutants that cause acid rain. Although primary responsibility for compliance lies with the states, the act also establishes a permit system for sources of air pollution such as power plants.

- The **Federal Insecticide, Fungicide, and Rodenticide Act** (FIFRA, 1972) regulates the sale and use of some 21,000 pesticides now in use in this country. Manufacturers must register a pesticide with the EPA before it is legal for use, and then it may be used only for the specific purpose for which it is labeled. Registration is contingent on the manufacturer's submitting scientific data on toxicity and environmental impact. **The Food Quality Protection Act** (FQPA, 1996) provides a major update of EPA responsibilities under FIFRA, including greater consideration of the risks of pesticide residues to children.

- **The Marine Protection, Research, and Sanctuaries Act** (MPRSA, 1972), also known as the **Ocean Dumping Act**, regulates the discharge of materials into U.S. ocean waters and authorizes related research. The act permits the EPA to phase out all ocean disposal of "harmful" sewage sludge and industrial waste, and to enforce such bans.

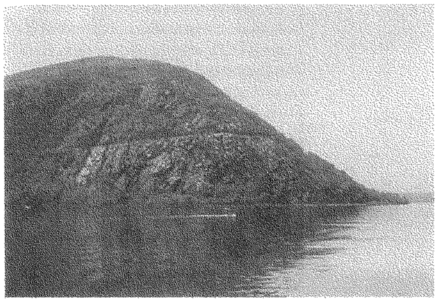
- **The Safe Drinking Water Act** (SDWA, 1974) is the primary legislation that ensures the quality and safety of the public water supply. The act establishes quality standards and treatment requirements. It also authorizes the EPA to regulate sources of contamination, and help states finance water quality projects.

- The **Resource Conservation and Recovery Act** (RCRA, 1976) permits the EPA to set standards, prohibit certain practices, and issue permits for facilities that generate or store hazardous or solid waste.

- The **Toxic Substances Control Act** (TSCA, 1976) allows the EPA to screen and regulate chemicals used in commerce. The EPA may require manufacturers to provide scientific information about a chemical's toxicity or harmful effects. Based on this information, the EPA may decide to impose any of a range of regulatory solutions, including use restrictions and outright bans, although the agency must use the least burdensome option that can reduce risks to a "reasonable level." TSCA, and later amendments, specifically require the EPA to control contamination from poly chlorinated biphenyls (PCBs), asbestos, radon, and lead.

- The **Environmental Research, Development and Demonstration Authorization Act** (ERDDA, 1976) provides the EPA with a statutory mandate to conduct basic and applied research on environmental topics, and to develop and demonstrate new technologies for monitoring, controlling, and cleaning up environmental contaminants.

- The **Clean Water Act** (CWA, 1977) sets ambitious goals for the quality of the nation's surface waters. The CWA requires treatment of all wastewater before discharge into waterways, with the goal of creating "swimmable" and "fishable" rivers and lakes. The act sets standards for "best practicable control technology" (BPT) and "best available technology" (BAT) for treating discharges. The act also provides for enforcement, and for assisting states and municipalities responsible for implementing it.



The successful battle to save New York's Storm King Mountain from the construction of a power plant set a legal precedent and opened the way for the National Environmental Policy Act (NEPA), the first of the many laws that govern the EPA.

- The **Comprehensive Environmental Response, Compensation, and Liability Act** (CERCLA, 1980), more commonly known as **Superfund**, authorizes cleanup of the most serious cases of existing hazardous waste pollution. The law creates a National Priority List of leaking hazardous waste dumps, spills, or other releases that can threaten the health of "any organism." The act establishes a "polluter pays" framework for funding site cleanup. An excise tax on petroleum and other chemicals originally covered the cost of cleaning up sites with no responsible party, but these taxes were not renewed after 1995, and the fund has had a zero balance since 2003.

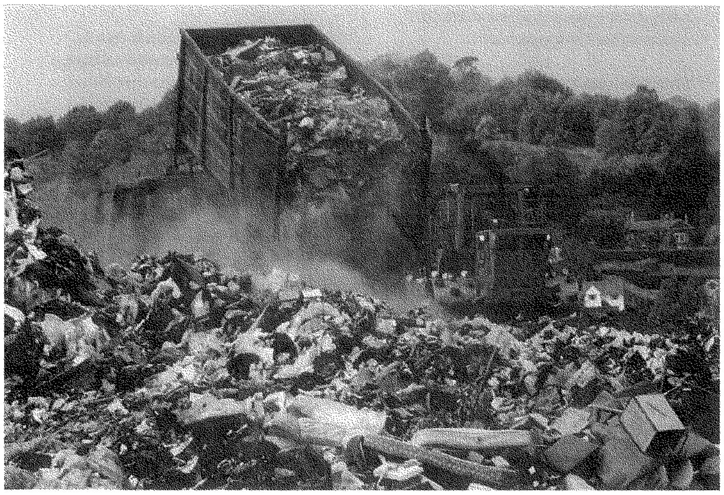
- The **Emergency Planning and Community Right-to-Know Act** (EPCRA, 1986) was signed into law after the Bhopal disaster in India, where release of toxic gas from an industrial plant resulted in the death of at least 3,000 people. EPCRA mandates annual reporting on the release or use of industrial chemicals through a database known as the Toxics Release Inventory (TRI), and also provides a national framework to enable local and state authorities to plan emergency responses to chemical accidents.

- The **Pollution Prevention Act** (PPA, 1990) mandates that the EPA establish programs and strategies to prevent pollution and reduce its sources. The act also requires annual reports on pollution prevention and recycling.

Other legislation addresses specific environmental contaminants (such as asbestos, lead-based paint in homes, and indoor radon), or issues for which the EPA does not have primary responsibility (such as the Endangered Species Act and the Occupational Safety and Health Act).

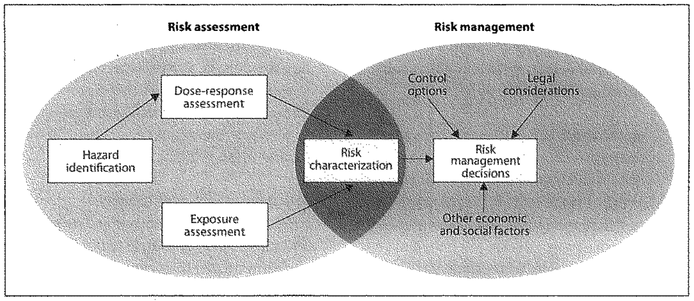
The Role of Science in the Policy Process

The EPA must rely on scientific information and expertise in fulfilling its mission. The most recent EPA strategic plan also lists "best available science" as a crucial strategy for achieving



The Resource Conservation and Recovery Act, enacted in 1976, charges the EPA with regulating solid waste disposal and storage.

FIGURE 1: **The EPA's Risk Assessment and Risk Management Paradigm**



Source: EPA's Office of Research and Development (EPA 2006a).

the agency's goals (EPA 2006a). Recognizing that the agency needs qualified scientific staff with the support of EPA leaders to fulfill this strategy, Administrator Carol Browner adopted the EPA Principles of Scientific Integrity in March ~~2000, to provide all employees with general~~ standards for scientific and intellectual conduct (EPA 2000). The quality of EPA science and its role in EPA decision making has also been the subject of numerous studies and reports, both internal (OIG 2002; EPA Expert Panel 1992) and external (for example, NRC 2000; Powell 1999). We found these reports helpful in interpreting the results of our investigations.

The EPA organizes much of its scientific and policy work around the principles of risk assessment and risk management (see Figure 1). This division creates a useful (although not always impermeable) barrier between scientific and policy decisions.

The goal of risk assessment is to gain a scientific understanding of the probability that populations exposed to a given hazard will be harmed, and to what extent. The resulting "risk characterization" draws on scientific knowledge of human exposure to the hazard and the dose-response relationship. While risk assessment is a scientific undertaking, it does involve making what the National Research Council, in its landmark 1983 study, called "science-policy choices"—that is, those that are not purely scientific, such as which model to use in predicting the effects of low doses of a hazard (NRC 1994; NRC 1983).

Risk management entails creating policies to address risks, and typically draws on many considerations beyond the scientific risk assessment, including legal considerations, stakeholder input, the technological feasibility of reducing risks, and other social and economic concerns. Such decisions are often ultimately based on the judgment of policy makers. However, some laws do provide specific guidance for how decision makers should or should not use science and technology in creating environmental policy. For example:

- **Best Available Science:** The Clean Air Act mandates that the EPA administrator issue National Ambient Air Quality Standards (NAAQS) that "accurately reflect the latest scientific knowledge," and that the EPA review those standards every five years. While the EPA has rarely kept to this schedule, this law has ensured that standards for six "criteria" air pollutants eventually reflect advances in scientific understanding. The Supreme Court has affirmed that the agency may not consider other factors when setting the NAAQS, such as technological feasibility or cost (*Whitman v. American Trucking Associations, Inc.* 2001). Statutory language of this type also appears in other environmental legislation, notably the Endangered Species Act.

- **Best Available Technology:** In regulating hazardous air contaminants, the CAA does not set absolute national standards, as in the case of the NAAQS, but rather requires polluting facilities to use the most up-to-date (or "maximum achievable") pollution control technology. Similar language regarding "best practicable" or "best available" technology can be found in the Clean Water Act's regulation of municipal and industrial discharges into the nation's waters, and in the Safe Drinking Water Act's regulations on drinking water contaminants.

- **Cost-Benefit Balancing and Market Failure:** Other environmental laws, notably FIFRA and TSCA, which regulate commercial products rather than "waste," require policy makers to balance costs and benefits before imposing regulations. President Bush's recent executive order 13422 further requires federal agencies to prove that regulations address a "market failure" (Bush 2007).

The Organization of the EPA

The EPA's broad legislative mandate translates into a large and complicated agency. The agency has some 18,000 employees, including 6,000 to 8,000 with scientific duties (OPM 2007). The agency is divided into 12 offices and 10 regions (see Figure 2a), and is headquartered in Washington, DC. Stephen L. Johnson is the EPA's eleventh and current administrator. The administrator is a member of the president's cabinet,

FIGURE 2A: **The EPA's 12 Central Offices and 10 Regional Offices**

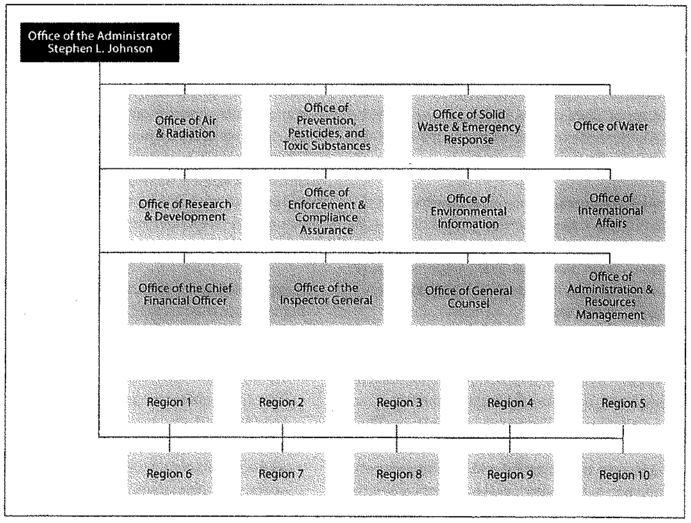
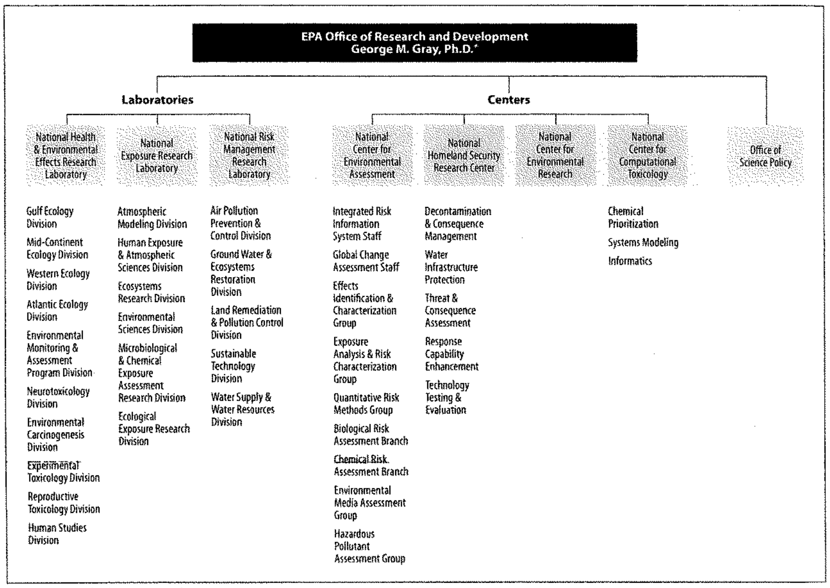

Office of the Administrator
Stephen L. Johnson
Office of Air & Radiation
Office of Prevention, Pesticides, and Toxic Substances
Office of Solid Waste & Emergency Response
Office of Water
Office of Research & Development
Office of Enforcement & Compliance Assurance
Office of Environmental Information
Office of International Affairs
Office of the Chief Financial Officer
Office of the Inspector General
Office of General Counsel
Office of Administration & Resources Management
Region 1
Region 2
Region 3
Region 4
Region 5
Region 6
Region 7
Region 8
Region 9
Region 10

FIGURE 2B: **The National Laboratories and Centers of the EPA's Office of Research and Development**


EPA Office of Research and Development
George M. Gray, Ph.D.*
Laboratories
Centers
National Health & Environmental Effects Research Laboratory
National Exposure Research Laboratory
National Risk Management Research Laboratory
National Center for Environmental Assessment
National Homeland Security Research Center
National Center for Environmental Research
National Center for Computational Toxicology
Office of Science Policy
Gulf Ecology Division
Mid-Continent Ecology Division
Western Ecology Division
Atlantic Ecology Division
Environmental Monitoring & Assessment Program Division
Neurotoxicology Division
Environmental Carcinogenesis Division
Experimental Toxicology Division
Reproductive Toxicology Division
Human Studies Division
Atmospheric Modeling Division
Human Exposure & Atmospheric Sciences Division
Ecosystems Research Division
Environmental Sciences Division
Microbiological & Chemical Exposure Assessment Research Division
Ecological Exposure Research Division
Air Pollution Prevention & Control Division
Ground Water & Ecosystems Restoration Division
Land Remediation & Pollution Control Division
Sustainable Technology Division
Water Supply & Water Resources Division
Integrated Risk Information System Staff
Global Change Assessment Staff
Effects Identification & Characterization Group
Exposure Analysis & Risk Characterization Group
Quantitative Risk Methods Group
Biological Risk Assessment Branch
Chemical Risk Assessment Branch
Environmental Media Assessment Group
Hazardous Pollutant Assessment Group
Decontamination & Consequence Management
Water Infrastructure Protection
Threat & Consequence Assessment
Response Capability Enhancement
Technology Testing & Evaluation
Chemical Prioritization
Systems Modeling
Informatics

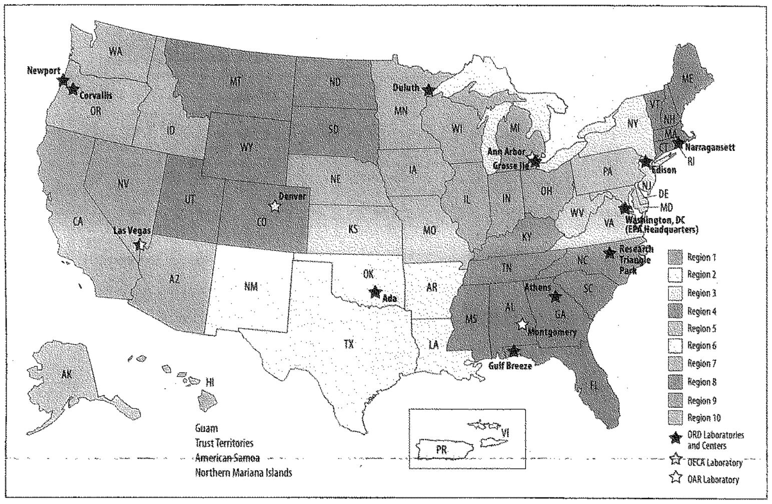
*George M. Gray is also the EPA science advisor.

although the EPA itself is not a cabinet-level agency.

Of the 12 program offices, seven contain the bulk of the agency's scientific expertise:

- The **Office of Air and Radiation** (OAR) is responsible for setting national air pollution standards in accordance with the CAA, as well as developing programs to address climate change, stratospheric ozone depletion, transportation and air quality, indoor air quality, and radiation exposure. The OAR also operates three research laboratories: the National Vehicle and Fuel Emissions Laboratory, the Radiation and Indoor Environments National Laboratory, and the National Air and Radiation Environmental Laboratory.
- The **Office of Prevention, Pesticides and Toxic Substances** (OPPTS) regulates and conducts research on pesticides and other toxic chemicals in the environment, as required by FIFRA and TSCA. The OPPTS also manages pollution prevention programs under the Pollution Prevention Act.
- The **Office of Solid Waste and Emergency Response** (OSWER) is responsible for managing the Superfund program and responding to releases of hazardous materials, administering the brownfields program and fostering

FIGURE 3: **Map of the EPA's 10 Regions and 16 Laboratories and Facilities**



redevelopment of contaminated sites, and developing guidelines for and regulating hazardous waste disposal.

- The **Office of Water** (OW) is responsible for ensuring the quality of groundwater and drinking water, overseeing wastewater treatment programs, and protecting watersheds, wetlands, and oceans under the CWA.

- The **Office of Research and Development** (ORD) is the research arm of the EPA, conducting basic and applied scientific research to support its programs. The ORD consists of a network of three national laboratories and four national centers that conduct scientific research, plus the Office of Science Policy (see Figure 2b, p. 17, and Figure 3). The two largest research facilities are in Research Triangle Park, NC, and Cincinnati, OH.

- The **Office of Environmental Information** (OEI) is charged with collecting and managing environmental information, and for ensuring its accuracy and reliability. The OEI also provides tools and resources to ensure public access to environmental information, such as the EPA's library network and its Toxic Release Inventory.

- The **Office of Enforcement and Compliance Assurance** (OECA) is responsible for enforcing the nation's environmental laws and helping the regulated community comply with regulations. The OECA also operates the National Enforcement Investigations Center Laboratory in Denver.

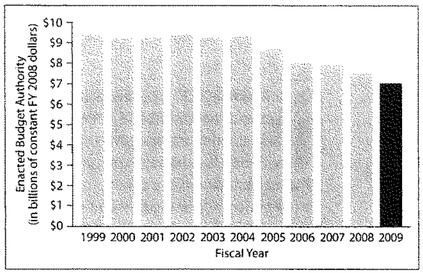
The Office of the Administrator is home to a number of divisions affecting the agency as a whole, including the Office of Children's Health

Protection and the Office of Civil Rights. The remaining five offices have comparatively few scientific responsibilities: the Office of the General Counsel, the Office of the Inspector General, the Office of the Chief Financial Officer, the Office of International Affairs, and the Office of Administration and Resources Management.

The EPA also has 24 official advisory committees, chartered under the Federal Advisory Committee Act, which provide external scientific advice. These committees include the Science Advisory Board, the Board of Scientific Counselors, and the Clean Air Science Advisory Committee (CASAC) (OCEM 2008). Various internal bodies also manage the EPA's generation and use of scientific information, including the ORD's Office of Science Policy, the Science Policy Council, and the Council on Regulatory Environmental Modeling (EPA 2006a).

Each regional office is responsible for implementing the EPA's programs within its geographic area (see Figure 3).

FIGURE 4: **EPA Budget 1999–2009**



Note: The EPA's discretionary budget, 1999–2009, is in billions of constant FY 2008 dollars. FY 2009 reflects the president's budget request.

Source: President's budget for fiscal year 2009, historical tables.

Funding Trends

The EPA's budget has declined in real terms by about 25 percent since fiscal year 2004—down from a level it had maintained since the 1990s (see Figure 4).

CHAPTER 3
Research Methods

In summer 2007, UCS sent a 44-question survey to almost 5,500 EPA scientists—a large fraction of the agency's 6,000 to 8,000 scientists (see more on the sample below). The survey asked these scientists about political interference in their work, the use of science in agency decision making, the EPA's effectiveness, employee morale, and other topics. The 1,586 scientists who responded were largely senior scientists: two-thirds had been with the EPA for 10 years or more, three-fourths had an advanced degree, and more than 80 percent were at General Service level 13 or higher.

UCS contracted with the Center for Survey Statistics and Methodology (CSSM) at Iowa State University to conduct the survey and tabulate and analyze the data. CSSM produced an online questionnaire that used anonymous logins and passwords to track which recipients had completed the survey, and to allow follow-up reminders to those who had not. Survey recipients received an initial email contact containing the login and password, as well as a hard copy mailed to their place of work. To boost the response rate, the researchers sent up to three reminder emails to those who had not responded.

To allow survey respondents to freely express their opinions about the EPA, our highest priorities were ensuring their confidentiality and anonymity. Thus, while UCS provided the sample of scientists that received the survey, we did not have access to any links between a given survey response and personal information, such as a name or email address. CSSM maintained such links solely to send out targeted reminder emails during the data collection period, and destroyed all such links once it closed the survey.

Creating the Survey Mailing List

No centralized directory of EPA scientists is available, so we drew on many sources to create the mailing list for the survey. Some offices and divisions list staff members online, and provide information on their job and project duties. Other divisions provided incomplete or no information about staff members online.

To fill these gaps, UCS asked current and former EPA employees to review staff lists from all remaining scientific offices and divisions, to identify scientists and exclude nonscientists. We also used targeted Internet searches to turn up information about employees' job titles and duties through lists of conference attendees, authors of peer-reviewed papers, internal memoranda, and newsletters. To allow as many EPA scientists as possible to participate, we erred on the side of including employees who worked at scientific branches and divisions even if their job duties were unclear.

The mailing list was therefore broad but of uneven quality. For example, in divisions that posted names but not job titles, the sample likely included some nonscientists. Conversely, the survey may have improperly excluded some legitimate scientists working in divisions where Internet search was the primary means of obtaining information. This approach also produced a notable bias toward agency veterans, as their names were more likely to appear on a website, at the expense of younger scientists and new hires. To address these shortcomings, we relied on several demographic questions in the survey itself to exclude nonscientists (see below).

Once we identified the names of EPA scientists, obtaining contact information was straightforward, as the online EPA Employee Locator provides telephone numbers, email addresses, postal addresses, and mail codes (EPA 2008c). We excluded anyone whose name did not appear in the locator from the mailing list.

Defining "Scientist"

We used a broad definition of "scientist" when compiling the mailing list. That is, we included Ph.D. scientists who had been promoted to policy-making positions and who no longer performed bench science, as well as individuals with a bachelor's degree whose daily work involves running experiments.

To confirm that we were surveying only agency scientists, we asked the recipients of the survey to identify their highest level of education, their major field of training, the percentage of their job duties that related to scientific topics, and what their EPA scientific work involved. We excluded the small number of respondents who indicated that zero percent of their job duties related to science from the sample.

Survey Questionnaire

The survey questionnaire featured 43 multiple-choice questions and one open-ended essay question. Besides posing demographic questions, the survey asked respondents about institutional support for scientists, agency culture and openness, employee morale and job satisfaction, the EPA's resources and effectiveness, the extent to which the policy-making process relied on science, and specific issues such as contracting and library closures.

The survey also asked respondents about their personal experiences with various forms of political interference in scientific work. And the open-ended essay question asked about how to improve the integrity of science at the EPA. (See Appendix A for the questionnaire and total responses, and Appendix B for further analysis of statistics in this report.)

Survey Demographics

CSSM mailed and emailed letters about the survey to 6,035 EPA employees beginning on June 25, 2007, and collected data until September 7, 2007. Email messages to 395 individuals bounced back as undeliverable; it is likely that these individuals are no longer EPA employees. CSSM also excluded 221 recipients judged to be nonscientists based on their personal communication or survey responses. Thus the eligible sample totaled 5,419 individuals (see Appendix D for a full methodology report from CSSM).

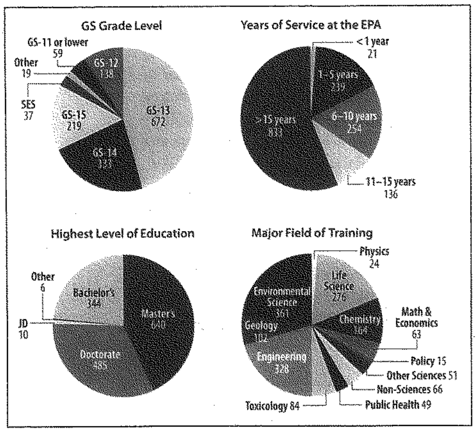
CSSM received completed surveys from 1,586 of these scientists, for a response rate of 29 percent (see Table 1). However, because of the unknown selection effects described above, the true response rate for EPA scientists is uncertain. Of the scientists who did respond, 855 answered the essay question.

The survey was designed to measure raw numbers of scientists who experienced political interference in their scientific work. Because of unknown selection effects in creating the sample, and the self-selection of respondents, it is difficult to extrapolate these raw numbers to a percentage of the EPA's total scientific workforce. Our analysis of the results includes percentages mainly as a tool for comparing scientists' responses to different options, and for comparing responses from different EPA offices and divisions.

TABLE 1: Summary of the Survey's Sample Size and Response Rate

	No.	Percent	No.	Percent
Total sample	6,035	100.0		
Ineligible	221	3.7		
No email available	395	6.5		
Total eligible sample	5,419	89.8		
Refusals			73	1.3
Unavailable for study duration			10	0.2
No response			3,750	69.2
Completed surveys			1,586	29.3
Response rate	29.3%			

FIGURE 5: **Basic Demographics of Survey Respondents**



To prevent anyone from identifying individual respondents from the data, we report results only for offices or divisions where 100 or more scientists received the survey.

Respondents included scientists from a broad range of disciplines (see Figure 5) working in every major office and subdivision of the EPA. Three-quarters (76 percent) held either a master's or doctoral degree, and a large majority (65 percent) spent more than half their time working on scientific topics. Nearly two-thirds (65 percent) were agency veterans with more than 10 years' experience at the EPA, and the vast majority (83 percent) were high-level government employees at General Service levels 13 through 15. Thirty-seven respondents were employees in the Senior Executive Service—scientists who serve in key positions just below the top presidential appointees.

The EPA's Response

In response to our initial email request, some EPA managers instructed their employees not to complete the survey, even though our cover letter indicated that they could do so on their free time or from a nonwork computer. However, after examining the project's methodology and goals, the deputy ethics officer of the EPA's Office of General Counsel circulated an email stating that the OGC had no legal concerns about the survey. The email affirmed that EPA employees could complete the survey on their personal time, and that doing so on their work computer would fall under the EPA's "limited use" policy. (See Appendix C for the initial emails and the response from the OGC.)

Interviews and Document Requests

To provide context for the survey results, we also interviewed 27 current and former EPA employees on scientific freedom at the EPA, and talked with three non-EPA scientists about their experiences working with EPA colleagues. The interviews focused on the sources' personal experience with political interference in their work, their perceptions of the agency's current and past work environment, and their recommendations for reform. We conducted most interviews via telephone, and most sources asked us not to name them in this report.

We also filed Freedom of Information Act (FOIA) requests for EPA documents on six topics: the closure of the OPPTS Chemical Library; the Toxics Release Inventory (TRI) burden reduction rule; the creation of the Endocrine Disruptor Screening Program (EDSP); the formulation of the Clean Air Mercury Rule; the formulation of the latest National Ambient Air Quality Standards for particulate matter, ozone, and lead; and the ability of climate change scientists to speak to the media and the public. As of press time, we had received complete responses to two of the FOIA requests (on the chemical library and TRI), two incomplete responses (EDSP and NAAQS), and no response to the remaining two requests. Multiple phone calls over six months to both the agency's chief FOIA officer and officials at the Office of Air and Radiation failed to secure timely release of the documents.

CHAPTER 4
Political Interference in Scientific Work

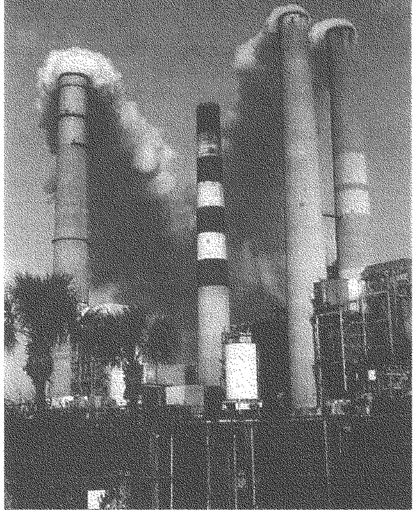
In responding to the survey, EPA scientists reported widespread and inappropriate interference in the agency's science by political appointees at the EPA, the White House, and other federal agencies. Such interference can be explicit—such as direct orders to alter scientific findings—or subtle, such as delays in the release of reports, or statements by EPA leaders that misrepresent scientific findings.

This chapter analyzes those survey findings. To provide context for them, we also summarize two widely reported cases of political interference in mercury regulations and climate change science, and also highlight a recent case involving interagency review of an EPA toxics database.

Survey Results

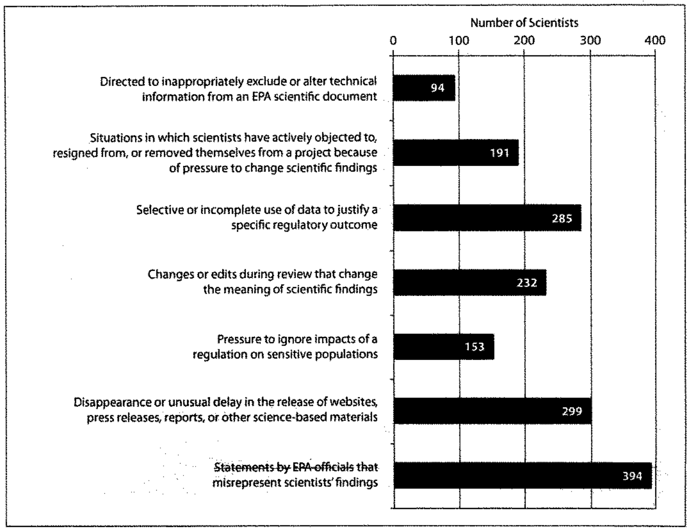
A series of questions asked respondents how often they had *personally experienced* various forms of inappropriate interference in their scientific work. (Response options included Frequently, Occasionally, Seldom, Never, and Not Applicable.) Large numbers of scientists reported direct and explicit interference:

- 94 scientists (7 percent of respondents) had frequently or occasionally been "directed to inappropriately exclude or alter technical information from an EPA scientific document." A total of 224 scientists (17 percent) reported that this occurred seldom or more often, indicating at least some experience with this most egregious form of interference.
- 191 scientists (16 percent) had personally experienced frequent or occasional "situations in which scientists have actively objected to, resigned from or removed themselves from a project because of pressure to change scientific findings." A total of 422 scientists (34 percent) reported at least some experience with this form of interference.
- 232 scientists (18 percent) had personally experienced frequent or occasional "changes or edits during review that change the meaning of scientific findings." A total of 482 scientists (38 percent) reported at least some experience with this form of interference.
- 285 scientists (22 percent) had personally experienced frequent or occasional "selective or incomplete use of data to justify a specific



After extensive White House interference, the EPA eased restrictions on hazardous emissions from coal-fired power plants, the primary man-made source of mercury in the United States.

FIGURE 6: **Number of EPA Scientists Reporting Various Forms of Political Interference**



regulatory outcome." A total of 532 scientists (42 percent) reported at least some experience with this form of interference.

- 153 scientists (13 percent) had personally experienced frequent or occasional "pressure to ignore impacts of a regulation on sensitive populations." A total of 311 scientists (26 percent) reported at least some experience with this form of interference.

Other questions asked respondents whether the agency had manipulated, delayed, or misrepresented science in more subtle ways (see Figure 6):

- 299 scientists (24 percent) had personally experienced frequent or occasional "disappearance or unusual delay in the release of websites, press releases, reports, or other science-based materials."
- 394 scientists (31 percent) had personally experienced frequent or occasional "statements by EPA officials that misrepresent scientists' findings."

Survey questions also asked respondents to specify how many incidents of interference they had experienced over the past five years (0, 1–5, 6–10, 11–20, or more than 20). A total of 889 scientists (60 percent) had personally experienced one or more such incidents. If each such incident was a distinct event, this represents at least 2,604 cases of political interference.

Nearly two-thirds of respondents (969 scientists, or 65 percent) have been EPA employees for more than 10 years. These agency veterans are uniquely able to judge whether this level of political interference is business as usual or whether interference has become more widespread. Among this subset, 409 scientists (43 percent) said interference had occurred more often over the past five years than during the previous five years. Only 43 scientists (4 percent) said interference had recently occurred less often. A total of 269 agency veterans (28 percent) said the level of interference had remained the same, while 240 (25 percent) said they didn't know.

Sources of Political Pressure

Other information from the survey provides more insight into how this interference occurs. These results show that (1) EPA scientists are under pressure from both internal and external influences; (2) pressure comes mainly from top political appointees and EPA leaders, not mid-level managers; and (3) percentages of scientists reporting interference vary widely across the agency.

The survey asked respondents about how many cases of various types they had encountered (options included Many, Some, Few, None, and Not Applicable):

- 516 scientists (43 percent) knew of "many or some" cases where political appointees at the EPA had inappropriately involved themselves in scientific decisions.

- 560 scientists (49 percent) knew of "many or some" cases where political appointees at other federal agencies had inappropriately involved themselves in EPA decisions. In their essays, nearly one hundred EPA scientists identified the White House Office of Management and Budget (OMB) as a primary culprit (see Box 1, p. 28).

- 507 scientists (42 percent) knew of "many or some" cases where "commercial interests have inappropriately induced the reversal or withdrawal of EPA scientific conclusions or decisions through political intervention." A smaller number of scientists (329, or 28 percent) reported such interference by non-governmental or advocacy groups.

Respondents expressed widespread respect for direct managers and supervisors but much less respect for the EPA's senior leaders. A total of 1,282 scientists (81 percent) respected the integrity and professionalism of their direct manager or supervisor, whereas only 686 (43 percent) said the same about senior leaders. A majority of respondents (906, or 59 percent) agreed that their direct supervisor stands behind staff members who take scientifically defensible positions that may be politically controversial.

> **Do not allow political appointees into the process of scientific review. Their job is to make management decisions, not influence the data and information before it is collected and presented.**
>
> A scientist from an EPA regional office

Regional Variations

Comparing responses from scientists at the agency's headquarters, 10 regional offices, and research laboratories adds another dimension to this analysis.

The percentage of scientists reporting political interference was highest at EPA headquarters in Washington, DC, and at the four program offices with regulatory responsibilities: the Office of Air and Radiation; the Office of Prevention, Pesticides, and Toxic Substances; the Office of Water; and the Office of Solid Waste and Emergency Response. A total of 337 scientists in these program offices (68 percent) and 379 scientists located in Washington, DC, at EPA headquarters (69 percent) reported at least one incident in the past five years (see Figure 7, p. 26).

Scientists reporting interference in the 10 regional offices ranged from 44 percent (region 6) to 73 percent (region 9). Within the Office of Research and Development, the National Health and Environmental Effects Research Laboratory

(NHEERL) was notably freer of interference than other divisions (39 percent), while the National Center for Environmental Assessment (NCEA) ranked among the worst (84 percent).

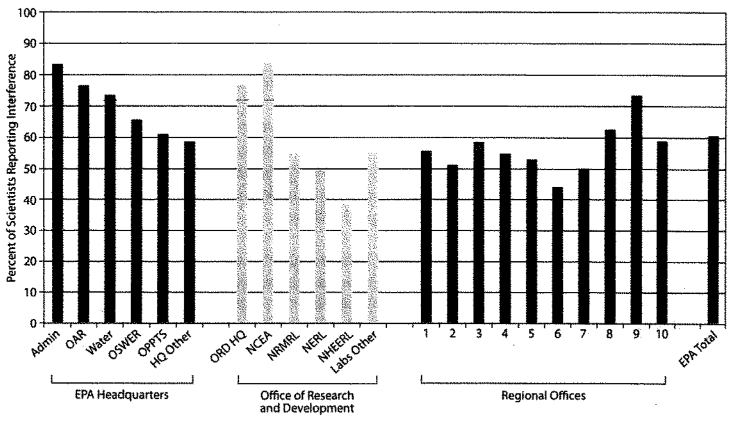
Figure 8 compares rates of seven types of interference between the program offices, the NCEA, and the NHEERL. Scientists at the NCEA reported high rates of all types of political interference in their work. NHEERL scientists reported far lower rates of the five most direct forms of interference than their colleagues elsewhere, and comparable (although still lower) rates of the two subtler forms of interference.

In their essay responses, more than 200 scientists said political interference was undermining the integrity of the EPA's scientific work.

Case Studies

Two recent cases of political interference—in the EPA's scientific work on mercury pollution and climate change—reveal most of these forms of interference: pressure to change methods and findings, direct editing of scientific documents by nonscientists, and delayed release of scientific reports. A third case illustrates the growing power of the Office of Management and Budget (OMB) and other federal agencies to interfere in the scientific work of EPA experts.

FIGURE 7: **Political Interference across the EPA over the Past Five Years**

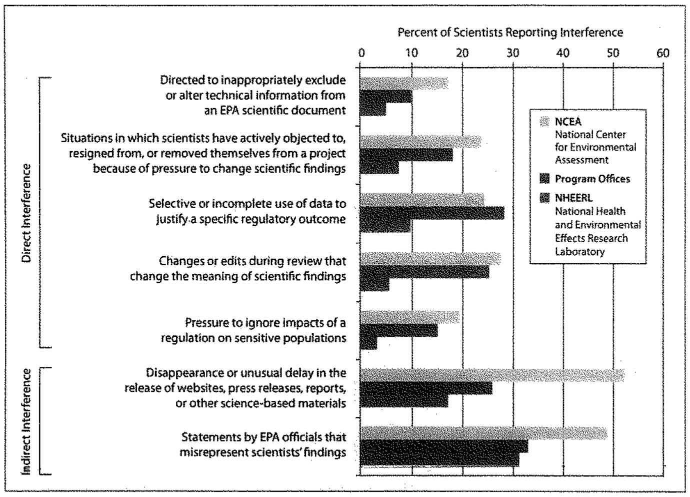


HQ	EPA Headquarters in Washington, DC
Admin	Office of the Administrator
OAR	Office of Air and Radiation
Water	Office of Water
OSWER	Office of Solid Waste and Emergency Response
OPPTS	Office of Prevention, Pesticides and Toxic Substances
ORD	Office of Research and Development
NCEA	National Center for Environmental Assessment
NRMRL	National Risk Management Research Laboratory
NERL	National Exposure Research Laboratory
NHEERL	National Health and Environmental Effects Research Laboratory

(see *http://www.epa.gov/epahome/locate2.htm* for full map)

Region 1	Maine, Massachusetts, Vermont, New Hampshire, Rhode Island, Connecticut
Region 2	New York, New Jersey, Puerto Rico, Virgin Islands
Region 3	Pennsylvania, West Virginia, Virginia, Delaware, Maryland, DC
Region 4	Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Alabama, Mississippi, Florida
Region 5	Minnesota, Wisconsin, Michigan, Illinois, Indiana, Ohio
Region 6	New Mexico, Texas, Oklahoma, Arkansas, Louisiana
Region 7	Nebraska, Iowa, Kansas, Missouri
Region 8	Montana, North Dakota, South Dakota, Wyoming, Utah, Colorado
Region 9	California, Nevada, Arizona, Hawaii, Guam, American Samoa, Northern Mariana Islands, Trust Territories
Region 10	Washington, Oregon, Idaho, Alaska

FIGURE 8: **Direct and Indirect Interference at EPA Offices and Labs**



The NCEA and NHEERL are in the EPA's Office of Research and Development. Rates of direct interference are consistently lower at the NHEERL than at the NCEA or the EPA's program offices, while rates of indirect interference are more comparable.

Regulating Mercury Emissions from Power Plants

On March 15, 2005, the EPA issued its final rule regulating mercury emissions from coal-fired power plants. The Clean Air Mercury Rule (CAMR) closely matched President Bush's Clear Skies proposal—a bill addressing several forms of air pollution that had failed to gain approval from a congressional committee in March 2005. The EPA's CAMR exempted power plants from standard Clean Air Act rules restricting emissions of hazardous air pollutants such as mercury in favor of a controversial cap-and-trade program.

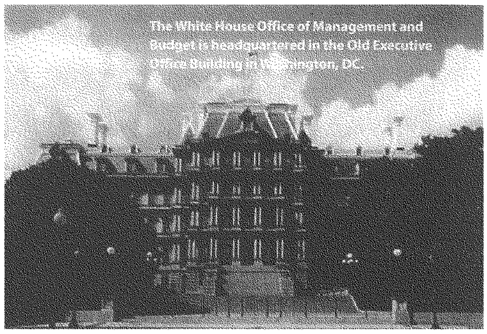
Bruce Buckheit, who retired in December 2003 as director of the EPA's Air Enforcement Division, attested that "the new mercury rules were hatched at the White House; the Environmental Protection Agency's experts were simply not consulted at all" (Buckheit 2004). Widespread evidence supports that claim:

- In 2002 a draft EPA report on children's health and the environment found that 8 percent of women of childbearing age had blood levels of mercury high enough to increase health risks to their children (EPA 2003). The *Wall Street Journal* reported in February 2003 that the report had been subject to an "unusual level of scrutiny by a half-dozen other federal agencies" (Fialka 2003). According to Dr. Tracey Woodruff, a former EPA scientist who worked on the report, EPA staff "spent an extended amount of time addressing questions and comments from the OMB and CEQ," and White House officials asked the agency to delete or modify specific text and topics (Woodruff 2008). After holding the report for nine months, the EPA released it in response to the *Journal* article.

continued on page 31

BOX 1: **The OMB Overrules EPA Science**

The White House Office of Management and Budget—especially its Office of Information and Regulatory Affairs (OIRA)—has played an increasingly powerful role in the creation, review, and approval of EPA decisions. Since the Reagan administration, the OMB has had the power to review and approve all government regulations, and to perform cost-benefit analyses. The OMB has used this power to force the EPA to modify or withdraw many rules and policies. For example, in 2002 the OMB thwarted an EPA plan to declare a public health emergency over asbestos found in the insulation of millions of homes across America (Schneider 2002).



The White House Office of Management and Budget is headquartered in the Old Executive Office Building in Washington, DC.

The OMB has recently stepped beyond its role in reviewing the EPA's policies to review and manage the actual science underlying them. For example, under former director John Graham, OIRA sought to create overly restrictive guidelines for how federal agencies should conduct scientific assessments, such as risk analysis and peer review of research.

The National Academies sharply criticized these guidelines as harmful to the mission of federal science and regulatory agencies, yet the OMB implemented them in modified form (UCS 2008). OIRA also recently hired a handful of scientists to create in-house scientific expertise in an office traditionally dominated by economists (OMB Watch 2003). The agency then began, for the first time, to review and criticize the scientific basis for EPA decisions.

In 2007, OMB analysts manipulated scientific knowledge about mortality arising from exposure to ground-level ozone, in the EPA's regulatory impact assessment on changing the ambient air quality standard for ozone (OMB Watch 2007; Patton 2007). The OMB has also interfered in the scientific basis for EPA policies on a 2004 rule regulating formaldehyde pollution from plywood plants (Miller and Hamburger 2004), and a 2006 decision not to tighten the ambient air quality standard for fine particulate matter (see Chapter 6). While the OMB's in-house expertise is undoubtedly helpful in interpreting scientific documents, it is inappropriate for the White House to second-guess the consensus of EPA specialists with decades of experience, and of advisory committees composed of internationally respected experts.

In the Scientists' Own Words

In their essays, nearly 100 EPA scientists explicitly identified the OMB's meddling in EPA decision making as a major hindrance to the agency's scientific integrity. Here is a small sample of responses to the question: "How could the integrity of scientific work produced by the EPA best be improved?"

Reviewing EPA Science

- "The unprecedented and unwarranted influence of the EPA's scientific work and findings by the White House and OMB must end."
- "OMB should stop interfering in EPA Science."

- "Get the White House, industry, and OMB out of what is supposed to be science-based decision making."
- "Also, for your next survey look at OMB. That is a true source of frustration. They truly interfere and want to stamp the White House Agenda over every document that is sent to them for review. Truly few realize the impact that they have. They have hired their own scientists and play the 'my scientist is better than yours' game. EPA has to accept a lot of **** from them to get any documents out."
- "OMB is increasingly interfering in earlier stages of projects (as opposed to review of draft documents and conclusions), sometimes insisting on methodologies that are less credible than those selected by EPA scientists."
- "Restrain [the] Office of Management and Budget. This Administration has not only watered down important rules protecting public health (I've see this happen firsthand with the PM 2.5 implementation rule), they have also altered internal procedures so that scientific findings are accorded less weight. For example, the staff paper used previously in setting the NAAQS review has been eliminated."
- "Get the OMB out of the business of reviewing science—they do not have adequate staff or adequately skilled staff to provide a scientific review of everything EPA does."
- "The role of OMB in terms of policy review and coordination is a problem. Economists, or whatever they are, 'playing' scientist and/or engineer is troublesome and a real annoyance. They lack the basic credentials to make scientific or engineering judgments."
- "Eliminate OMB and CEQ interference in EPA science, prevent political appointees from inserting themselves into controversial science issues."
- ~~"Get OMB and their inexperienced~~ staff ~~out of the review and decision-making process. They create~~ time delays and have inappropriately stopped agency work that has been in progress for years due to their lack of scientific understanding."
- "When I was first at EPA (1988), we did good work but it was sometimes ignored. That was frustrating, but at least the work was there. Now it seems like they want the scientific work to match the preordained conclusions. In case you are wondering, I think peer review is a good thing—I've seen people too invested in their beliefs to see what their data are really saying. But OMB, with John Graham at the helm, seemed intent on rendering EPA and every other regulatory agency (Food and Drug Administration, Occupational Safety and Health Administration, Mine Safety, Consumer Product Safety Commission...) utterly powerless with its 'information quality guidelines.' And although the administration chose Steve Johnson (a career scientist) as EPA administrator, it sent Graham henchman Marcus Peacock over to keep a close eye on EPA as deputy administrator."

[The White House Office of Management and Budget] and the White House have, in some cases, compromised the integrity of EPA rules and policies; their influence, largely hidden from the public and driven by industry lobbying, has decreased the stringency of proposed regulations for non-scientific, political reasons. Because the real reasons can't be stated, the regulations contain a scientific rationale with little or no merit.

A scientist from an EPA regional office

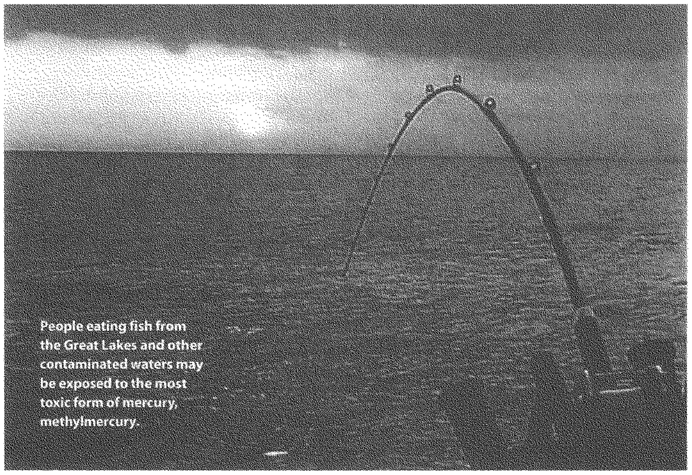
- "OMB and the White House have, in some cases, compromised the integrity of EPA rules and policies; their influence, largely hidden from the public and driven by industry lobbying, has decreased the stringency of proposed regulations for nonscientific, political reasons. Because the real reasons can't be stated, the regulations contain a scientific rationale with little or no merit."
- "Get OMB out of the risk assessment business. They aren't qualified and do their best to compromise EPA's process and drag out actions based on EPA's determinations. Demanding that things be referred to [the National Academies], which inevitably slides any decision out 3–4 years, is one of OMB's favorites."

Lessening EPA Independence

- "Currently, OMB is allowed to force or make changes as they want, and rules are held hostage until this happens. OMB's power needs to be checked as time after time they weaken rulemakings and policy decisions to favor industry."
- "Stop allowing political employees and OMB to 'regulate' what EPA scientists do. Just let EPA scientists do their job; we are well qualified and can be trusted."
- "In this administration, self-censorship is almost as powerful as political censorship. Options that OMB or the White House wouldn't like aren't even put forward."
- "The current administrator is a puppet operated by CEQ and OMB."

Transparency

- "Reduce the power of OMB over EPA scientific products. All communications between EPA and OMB during the development of agency technical products and actions should be preserved for the public record. Stakeholders should demand an end to 'paralysis by analysis' strategies to prevent EPA from doing its job. In particular, implementation of OMB's risk assessment guidelines would be disastrous."
- "Require more transparency regarding involvement of OMB, CEQ, and other federal agencies when they comment [or] pressure EPA to make revisions in proposed and final actions."
- "Over the last few years it has come to pass that OMB typically provides nonsensical political edits to every technical guidance coming out. (Not just the ones we hear about in the news, but ALL of them.) This is often done behind closed doors—after the document leaves the control of technical staff, OMB/ White House request EPA management to make their requested political changes as EPA technical edits, before officially submitting to OMB for review."
- "Integrity of scientific work is high. OMB has been 'granted' authority beyond what I understand has been traditional to impact final decisions. It is not clear who, how, or what initiated this change or increase in power, but it is absurd. A nonscientific body that does not have legal deference is forcing final decisions that may not be palatable to staff, and even political officials at EPA. Watch out for this on the upcoming ozone NAAQS decision. Solution: OMB must not step beyond its authority, and return to traditional review of regulations."
- "Reduce influence of White House and OMB in decision making. Recognize [that] costs of new regulations are easy to estimate, while costs of improvements in health and the environment are much more difficult."
- "Limit OMB review of, and influence on, content of scientific/engineering data and information (e.g., in rulemaking and guidance development). 2.) Require more transparency in OMB review process. 3.) If we are going to have to justify all environmental policy/regulations/guidance through cost-benefit, allow us to develop methodologies to quantify nonuse and ecological benefits."
- "Control the power of OMB to a reasonable level—OMB does more to waste time and taxpayer dollars than any other organization in the government."



People eating fish from the Great Lakes and other contaminated waters may be exposed to the most toxic form of mercury, methylmercury.

~~continued from page 27~~

- As an alternative to Clear Skies, Senators Thomas Carper (D-DE), Judd Gregg (R-NH), Lamar Alexander (R-TN), and Lincoln Chafee (R-RI) proposed a measure to control carbon dioxide, sulfur dioxide, and nitrogen oxides in addition to mercury. The EPA evaluated this proposal, but withheld its analysis from the senators. Several months before the EPA finally released its evaluation, an internal agency briefing was leaked to the *Washington Post* (Gugliotta and Pianin 2003). In the briefing, the EPA concluded that the Senate proposal would cut the three pollutants earlier and more deeply than the Clear Skies Act, result in 17,800 fewer expected deaths by 2020, and reduce carbon dioxide emissions at "negligible" cost to industry. EPA staff members recounted that at a May 2003 meeting on the unreleased report, Jeffrey Holmstead, then administrator of the agency's Office of Air and Radiation (OAR), asked, "How can we justify Clear Skies if this gets out?" Holmstead has since stated that he did not "recall making any specific remarks" (Lee 2003).

- Five career EPA employees told the *Los Angeles Times* that they had been instructed not to conduct the required scientific and economic studies comparing the new Clear Skies proposal with other regulatory options, despite requests from a federal advisory committee. William Wehrum, a senior OAR advisor, told staffers that such comparative studies would be "postponed indefinitely," and two staffers said Holmstead told them in early 2003 that "the studies would not be conducted partly because of 'White House concern'" (Hamburger and Miller 2004).

- Instead of input from the EPA's scientific staff, the initial CAMR proposal included significant input from power companies and utilities affected by the rule. The proposal lifted several paragraphs verbatim from memos prepared by Latham & Watkins, a law firm representing the utility industry, and the previous employer of both Holmstead and Wehrum (Pianin 2004). Language setting the standard for estimating power plant emissions came from West Associates, an advocacy group representing 20 power and transmission companies (see Appendix G of Jeffords et al. 2004.) EPA officials claimed the language was inserted during the "interagency process."

- EPA Inspector General Nikki Tinsley confirmed in February 2005 that EPA scientists were pressured to change their analyses and findings to support a predetermined value for a national cap on mercury emissions (OIG 2005). The Government Accountability Office also found that the EPA's rulemaking process did not include adequate studies comparing different proposals, and did not "estimate the value of the health benefits directly related to decreased mercury emissions" in conducting its cost-benefit analysis (GAO 2005). The EPA also excluded a Harvard study—funded by the EPA and coauthored by an EPA scientist—that found health benefits 100 times larger from adopting stricter mercury regulations (Vedantam 2005).

> **Currently, [the White House Office of Management and Budget] is allowed to force or make changes as they want, and [EPA actions] are held hostage until this happens. OMB's power needs to be checked as time after time they weaken rulemakings and policy decisions to favor industry.**
>
> A scientist from the Office of Air and Radiation

The EPA's own Children's Health Protection Advisory Committee found the proposed mercury rule inadequate, stating that it does "not go as far as is feasible to reduce mercury emissions from power plants, and thereby does not sufficiently protect our nation's children" (CHPAC 2004). In February 2008, a federal appeals court ruled that the CAMR violated the Clean Air Act by exempting power plants from stricter regulations governing hazardous air pollutants (Pasternak 2008).

Editing the Science of Climate Change

The Bush White House, through political appointees at the OMB and the CEQ, has a long track record of tampering with the EPA's scientific documents on climate change. A few examples of this high-level interference:

- The 2002 U.S. Climate Action Report, prepared by the EPA to fulfill the United Nations Framework Convention on Climate Change, was unusual for the administration in that it explicitly called human activity the cause of climate change, and described specific problems that global warming would bring to the United States (Revkin 2002). The report recommended adapting to these problems rather than attempting to lower emissions. Although all relevant agencies approved the report, the administration issued no announcement when sending it to the United Nations. When journalists asked President Bush about it, he dismissed it as "a report put out by the bureaucracy" (Seelye 2002).

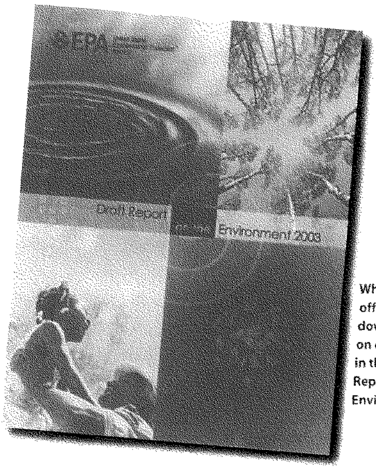
- In September 2002, the White House removed a section on climate change from the EPA's annual report on air pollution (EPA 2002), even though the five previous reports had addressed the topic. An investigation by Rep. Henry Waxman (D-CA) uncovered emails from CEQ chief of staff Philip Cooney showing that CEQ had "vetoed" the entire climate change section (Waxman 2007).

- In June 2003, the *New York Times* reported that the White House had tried to substantially alter the section on climate change in the EPA's draft Report on the Environment (EPA 2003; Revkin and Seelye 2003). Administration officials, including Cooney, demanded that the EPA remove reference to a temperature record covering 1,000 years, statements referencing numerous scientific studies showing that human activity is contributing significantly to climate change, and a summary statement that "climate change has global consequences for human health and the environment."

Cooney also inserted references to a study by Willie Soon and Sallie Baliunas, funded by the American Petroleum Institute, disputing the scientific consensus on climate change. In an April 21, 2003, memo to Kevin O'Donovan in the Office of the Vice President, Cooney noted that, "CEQ just inserted a reference to [Soon and Baliunas] in the final draft chapter on global climate change contained in EPA's first 'State of the Environment' report. . . . With both the National Academy and IPCC (Intergovernmental Panel on Climate Change) holding that the 20th Century is the warmest of the past thousand years (see below), this recent study begins to provide a counterbalance on the point to those two authorities" (Waxman 2007).

According to an internal EPA memo, White House officials demanded that the report include so many qualifying words—such as "potentially" and "may"—that it would have implied "uncertainty . . . where there is essentially none." Jerry Mahlman, a former official of the National Oceanic and Atmospheric Administration who served as a reviewer for the EPA report, noted in an interview with UCS, "It was obvious that senior EPA officials felt compelled to water down the conclusions" (Mahlman 2006). In the end, the report released for public comment lacked the entire section on climate change. According to internal EPA documents and UCS interviews, agency staff members chose this path rather than compromise their credibility by misrepresenting the scientific consensus (Anonymous EPA staff members 2004; EPA internal memo 2003).

- The EPA's climate change website remained virtually unchanged from 2002 to 2006 (Piltz 2006a). The agency finally posted a new website on October 19, 2006 (EPA 2008d). The ~~new site includes accurate scientific informa~~tion on climate change, but it lacks references to important reports such as the National Assessment of Climate Change Impacts and the U.S. Climate Action Report (Piltz 2006b). As of April 2008, the site also prominently features a discussion of uncertainty in climate change science.



White House officials watered down a section on climate change in the EPA's Draft Report on the Environment.

- In July 2002, CEQ official Sam Thernstrom edited an op-ed by EPA Administrator Christine Todd Whitman scheduled to appear in *Time* magazine. Thernstrom inserted the claim that signing the Kyoto Protocol would put 5 million Americans out of work. EPA Associate Administrator Tom Gibson objected that the figure assumed unrealistic implementation of the protocol, and that "it is also the high end of the numbers that were expressed as a range." Thernstrom consulted with CEQ chief of staff Cooney and CEQ head James Connaughton, and quickly replied that "the figure is taken directly from the President's 2-14 speech, and Jim Connaughton's Senate testimony last week. Using merely an abstract dollar figure may not be as compelling" (Waxman 2007).

Administrator Whitman removed the offending statistic later that day, but the CEQ apparently overruled her. Published in *Time* on August 26, 2002, the op-ed claimed that "Kyoto would put millions of Americans out of work." According to the Waxman report, CEQ officials were still making such inflated claims as late as 2005.

My opinion of EPA has changed since being here. Specifically, I had believed EPA was more scientific in its approach. Now I realize that EPA has politically driven agendas that sometimes, not always, affects decisions of scientific nature.

A scientist from an EPA regional office

Interagency Review of the IRIS Database

Today the Department of Defense (DOD) and other federal agencies are seeking greater control of the scientific information in the EPA's Integrated Risk Information System (IRIS), which includes toxicology profiles on more than 500 chemicals. A new framework would allow the OMB, the National Aeronautics and Space Administration (NASA), the Department of Energy, and the DOD to declare certain chemicals "mission critical," and to require additional or modified studies (Inside EPA 2007a). This additional analysis could add years of delay to the release or updating of information on chemicals posing a significant threat to public health. Because federal agencies are often part of the regulated community, such a review would also institutionalize second-guessing of EPA science by conflicted third parties.

For example, information from IRIS on the toxicity of perchlorate could mean that the DOD and its contractors are liable for potentially billions of dollars in cleanup costs. The DOD has long sought to weaken any scientific standard that would mandate cleanup of perchlorate contamination (Sass 2004). After the EPA's initial 2002 perchlorate assessment, the DOD criticized the EPA's science, and lobbied to have the National Academies review the subject. Air Force Col. Daniel Rogers linked the outcome of scientific deliberations to national security, claiming before the resulting National Academies panel that "every additional layer of science-policy precaution embedded into this risk assessment comes at the expense of the [Defense] Department's ability to acquire and test propulsion and weapons systems" (Hogue 2003).

The National Academies panel eventually proposed a perchlorate standard weaker than the EPA's initial risk assessment. The EPA has not yet finalized a drinking water standard for perchlorate.

The EPA has also recently proposed that it no longer include numerical assessments of toxicity in its draft reports on IRIS chemicals. This would be a major blow to the public and other regulatory agencies, which often rely on draft reports for information on these chemicals while waiting for the final reports—which can take several years (Inside EPA 2007b).

Finally, the OMB reviews the "charge" to scientific panels that provide peer review of IRIS risk assessments. The charge determines the questions a panel will answer during its investigation. An independent scientist (name withheld by request) reported that the OMB modified the charge to one such panel by removing questions asking whether the risk assessment adequately addressed public health risks, and adding questions asking if the EPA had gone too far in its risk assessment. The scientist stated that OMB's substitution "served to downplay the risk posed by the chemical in question" (Anonymous scientist 2008).

BOX 2: **More Examples of Political Interference in EPA Science**

The examples of political interference described here represent only a small portion of the problems UCS has documented at the EPA. Our online *A-to-Z Guide to Political Interference in Science* fully describes several other incidents of politicization of EPA science, with references and links to primary documents.* These additional incidents include:

- **Air Pollution Monitoring:** The EPA allowed North Dakota to alter the way it measured air quality in 2004, thus bringing Theodore Roosevelt National Park into compliance with air quality standards without actually reducing pollution.

- **Atrazine:** Despite compiling hundreds of pages of evidence documenting the harmful effects of atrazine, a common weed killer, the EPA refused to regulate the herbicide. Challenges from industry groups to scientific studies documenting atrazine's harmful effects, as well as closed-door meetings with industry representatives, led to the controversial decision.

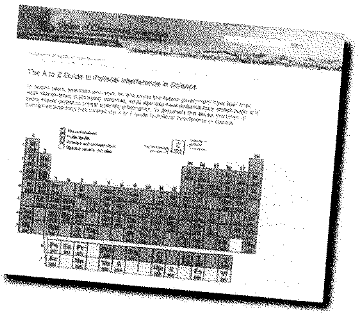
- **Fuel Efficiency:** In 2005 the EPA made a last-minute decision to delay the release of its annual report on automotive fuel efficiency until after a final vote in Congress on a bill addressing fuel efficiency standards.

- **Pesticides:** Unions representing 9,000 EPA employees charged the EPA with relying too heavily on industry studies and opinions in reviewing thousands of pesticides under the Food Quality Protection Act.

- **Plywood Plant Pollution:** The OMB distorted scientific information on the risks of formaldehyde exposure to support a weakening of the EPA's regulation of harmful emissions from plants that manufacture plywood.

- **Selenium Contamination:** In 2004 the EPA misrepresented research on the toxic effects of selenium on fish populations in setting a selenium standard that many scientists felt could be devastating to stream ecosystems.

- **Ground Zero Air Quality:** In a series of public statements issued after the terrorist attacks of September 11, 2001, the EPA assured the people of New York that the air around ground zero was safe to breathe. However, the agency lacked authoritative information on which to base this reassuring public posture—and even ignored internal data conflicting with it.



The A to Z Guide to Political Interference in Science

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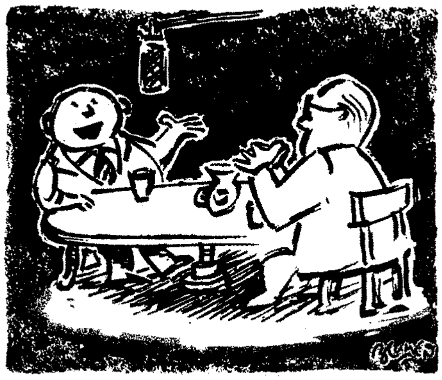
* See *http://www.ucsusa.org/AtoZ.*



"Well, Jim, I got into politics to raise standards. Mercury standards, air pollution standards...you name it!"

Discussion

In 1992 the EPA report *Safeguarding the Future: Credible Science, Credible Decisions* identified the problem of political interference in the agency's work succinctly: "Science should never be adjusted to fit policy. Yet a perception exists that EPA lacks adequate safeguards to prevent this from occurring" (EPA Expert Panel 1992). Our findings show that the problem persists more than 15 years later.

Hundreds of scientists across the agency report personal experience with many forms of interference, from explicit directives to change scientific findings to excessive delay in the release of such information. These numbers should be zero. The survey results indicate that the EPA, like so many other federal agencies, is weathering a storm of interference in its scientific work.

While the EPA has never been entirely free of politicization, agency veterans attest that such interference has worsened in the past five years. This finding is supported by a recent decision by the coalition of unions representing 10,000 EPA employees to withdraw from a 1998 cooperative agreement with EPA management. In a letter to Administrator Johnson, union leaders cited numerous recent examples of political interference in the work of EPA employees, and the agency's refusal to recognize its own Principles of Scientific Integrity as a basis for employee grievances (EPA Labor Union Coalition 2008; EPA 2000).

Survey results from NHEERL scientists indicate that a high level of interference in scientific work is not an inevitable consequence of scientific work or ordinary workplace conflicts. A comparison between the EPA's basic science offices and its program offices shows that interference arises much more often during the process of crafting regulations. Regulations have political and economic impacts, and powerful interests are invested in the outcome of agency decisions. Indeed, large numbers of survey respondents identified political appointees and industry groups as responsible for this interference.

Over the past few years, the OMB and the CEQ have moved beyond reviewing EPA policies and regulations to reviewing and second-guessing the underlying scientific determinations—a fact that more than 100 respondents explicitly noted in their essays. Philip Cooney's edits are only the most well-known breach of the wall between science and policy (see Boxes 1 and 2). For example, the president's recent executive order 13422 extends OMB review to a larger swath of scientific documents, including risk assessments, and gives political appointees in each agency the power to halt proposed regulations before they are announced publicly (Bush 2007). This shift is part of a broader centralization of decision making under the Bush White House that has far-reaching consequences for scientific integrity.

Interagency review of the EPA's IRIS database highlights the extent to which science has become the preferred battleground for tough policy questions. Exempting the DOD and other agencies from the cleanup of environmental pollution may sometimes be in the nation's best interest, but such an exemption should be an explicit policy decision. Manipulating scientific data to support such a decision is unacceptable. IRIS is a scientific database that serves as a source of objective information for protecting public health and the environment, including developing regulations, enforcing environmental laws, and assessing environmental cleanup efforts. Sullying this database through political interference does a serious disservice to the scientists working with the IRIS data and to the public.

To prevent such political review from becoming more widespread, the EPA needs to be empowered to be the lead environmental agency. A 2002 GAO report found merit in the idea of elevating the EPA to a cabinet-level agency. The report urged policy makers to consider that:

> "(1) environmental policy be given appropriate weight as it cuts across the domestic and foreign policies that other ~~Cabinet departments implement and~~ enforce and (2) the head of the agency is able to deal as an equal with his or her counterparts within the federal government and within the international community as well. Providing Cabinet status would also clarify the organization's direct access to the President on environmental matters" (GAO 2002).

Of course, science is not the only element underpinning good policy making. However, without strong institutional safeguards, decision makers will always be tempted to shore up a given policy by manipulating the underlying science. The EPA must maintain a firewall between science and policy. And no matter what the ultimate outcome, the decision-making process must be transparent: the agency must publicly release *all* relevant scientific findings.

Given the complexity of today's environmental challenges, from toxics to climate change, a strong and credible EPA is critical. Political interference in the agency's scientific work damages its credibility, makes government less accountable to its citizens, and has serious effects on the health, safety, and security of the American public.

Political considerations should not trump environmental stewardship, and the EPA should not be forced to be silent on the environmental consequences of policy shifts.

A scientist from an EPA regional office

CHAPTER 5

Barriers to the Free Communication of Science

Free communication of the results of scientific research is a critical element of the scientific process—as George Gray, the EPA's science adviser and the assistant administrator of its Office of Research and Development (ORD), acknowledged at a recent scientific meeting. Gray stated that the ORD has "absolutely no policies that prohibit in any way someone's ability to publish their research or to talk to the media" (Gray 2008).

The scientists who responded to our survey had a less positive view of EPA policies on public communication of research. A majority felt they could not speak freely to the news media. And a smaller but significant number reported barriers to publishing in peer-reviewed journals.

Survey Results

Large numbers of EPA scientists report that the EPA's policies restrict the free communication of scientific information. These scientists report problems with both the communication of scientific results to the media and publication in peer-reviewed journals (see Figure 9):

- 783 scientists (51 percent) disagreed or strongly disagreed that EPA policies allow scientists to "speak freely to the news media about their findings." Another 556 scientists had no opinion or were unsure (36 percent). Only 197 scientists (13 percent) agreed that the EPA allows scientists to communicate freely with the media.

  Respondents from the ORD (267 scientists, or 67 percent)—especially its National Center for Environmental Assessment (NCEA) (39 scientists, or 78 percent within that center)—were more likely than scientists in other EPA divisions to report restrictions.

- 291 scientists (24 percent) disagreed or strongly disagreed that they are "allowed to publish work in peer-reviewed scientific journals regardless of whether it adheres to agency policies or positions." Agency veterans with more than 10 years of experience at the EPA were slightly more likely (26 percent) than other scientists to disagree with the statement.

This rate was slightly higher for the ORD (101 scientists, or 26 percent), and nearly half of NCEA respondents disagreed with the statement (24 scientists, or 47 percent). As with political interference in scientific work, the contrast with the ORD's National Health and Environmental Effects Research Laboratory was striking: only 18 of 128 scientists (14 percent) from the NHEERL disagreed with the statement.

Beyond restrictive policies, hundreds of scientists also fear retaliation for speaking candidly about the EPA's work:

- 382 scientists (24 percent) disagreed or strongly disagreed that they could openly express concerns about the EPA's work *outside* the agency without fear of retaliation.
- 492 scientists (31 percent) disagreed or strongly disagreed that they could openly ~~express concerns about the EPA's work~~ *inside* the agency without fear of retaliation.

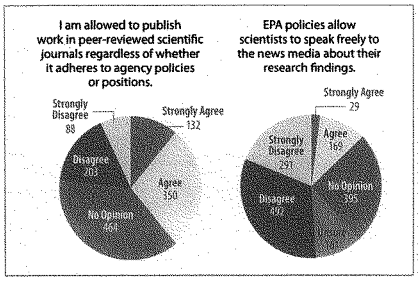
The combination of political interference in science (explored in Chapter 4) and barriers to the free communication of scientific findings affects the amount and quality of information that the EPA provides to the U.S. public:

- 88 scientists (7 percent) had frequently or occasionally been directed to "provide incomplete, inaccurate, or misleading information to the public, media, or elected officials," while 123 (9 percent) had frequently or occasionally felt an implicit expectation to do so.
- While nearly half of respondents agreed or strongly agreed that the EPA "routinely provides complete and accurate information to the public," 357 scientists (23 percent) did not.

Case Studies

Interviews with current and former EPA scientists provide some explanation for the gulf between Dr. Gray's statements and the perceptions of many rank-and-file scientists. These interviews show that although the EPA's policies may reflect a rhetorical commitment to openness on peer-reviewed publications, presentations at scientific conferences, and media interviews, these policies do not reflect actual practice. As one ~~former EPA scientist (name withheld by request)~~ put it, "I was never told not to speak to the press, but conventional understanding in the agency was that it is not a good idea to do so, and that it could harm your career if you did" (Anonymous former EPA scientist 2008).

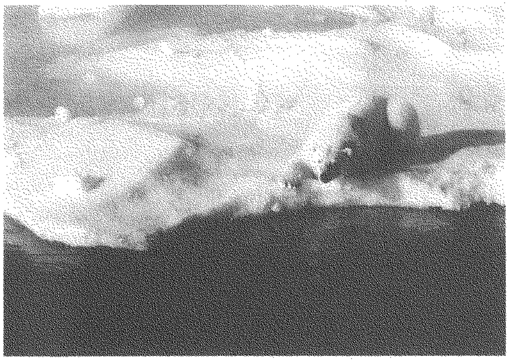
FIGURE 9: **Scientists' Perceptions of the EPA's Communications Policies**



The same scientist reported that agency employees are "typically required to route media requests through the press office." This scientist described one interaction with the media after a public talk:

> "A reporter called to follow up and I was asked to refer her to the press office. The press office didn't know what her line of questioning would be and they were nervous about what she would ask. This ended up delaying the interview. The reporter was persistent and the time delay made her suspicious the EPA was hiding something, so it ended up backfiring. Eventually I did the interview with two public affairs officers on the phone" (Anonymous former EPA scientist 2008).

A 2002 survey of the EPA's 10 regional offices by the Society of Environmental Journalists found a wide range of official and unofficial policies on scientists' contact with the media (Cooper 2002). Some regions required employees to route all media requests through the Office of Public Affairs, while other regions simply asked employees to inform the OPA about interviews that had occurred. Some regions had written policies, while others operated informally.



More recent evidence indicates that some regions and divisions do not allow scientists to speak freely to the media. A 2004 memo from acting region 5 Administrator Bharat Mathur stated:

> "If you receive any request for information or an interview from a member of the media, you should refer the caller to OPA.... Please refrain from answering such inquires [sic] directly. OPA will determine the appropriate response and who should respond after consultation with program staff, and if necessary, after elevating issues for senior-level attention" (Mathur 2004).

The ORD sent a similar directive requiring employees to route media interviews through the OPA to all staff in 2006 (Brown 2006).

Communicating the Science of Climate Change

Atmosphere of Pressure, a 2007 report by UCS and the Government Accountability Project (GAP), found widespread interference in the ability of federal scientists studying climate change to communicate their research findings. Muzzling of climate scientists was found to be especially intense at the National Oceanic and Atmospheric Administration and the National Aeronautics and Space Administration, but similar problems were reported at five other federal agencies, including the EPA (UCS and GAP 2007).

Recent examples of problems with the free communication of climate change research at the EPA include the following:

- In the fall of 2006, EPA managers barred an agency scientist from giving an invited talk at a conference on soil science, because the ~~topic involved the politically~~ sensitive subject of climate change. The EPA eventually allowed the talk to proceed after protests and intervention by the session organizers.

  A colleague of the scientist in question, who does not work for the EPA and asked to remain anonymous, described the events leading to the talk. Session organizers invited the EPA scientist—an acknowledged leader in the field—to give the talk, and he accepted. Several months later the scientist notified the organizers that he would have to withdraw because he received word from his supervisor that the EPA would not approve travel for scientists in his division to make presentations related to climate change or atmospheric ozone (Anonymous non-EPA scientist 2007).

  Concerned that this was inappropriate and possibly a miscommunication, session organizers contacted a higher-level manager at EPA headquarters. The organizers warned that if the agency did not approve the talk, they would announce that fact to conference attendees, and observe "20 minutes of silence" when the scientist had been scheduled to speak. The EPA then approved the talk.

- Another EPA scientist, also on condition of anonymity, reported being unable to present research results related to climate change at two scientific conferences in the past few years (Anonymous EPA scientist 2007).

- Other EPA climate scientists have encountered restrictions on media contact even when they do give interviews. In June 2006, Cornelia Dean of the *New York Times* reported that Dr. James Titus, EPA project manager for sea level rise, could no longer publicly discuss issues such as beach erosion, and that he had to route all such questions through the EPA's press office. The office referred Dean's requests for on-the-record information to William Wehrum, then acting assistant administrator for the EPA's Office of Air and Radiation (Dean 2006).

  In September 2006, the agency allowed Titus to do an interview on the radio show *Earthbeat*, but with significant restrictions (Maassarani 2007). During the interview, host Mike Tidwell told Titus that the show's producer, Aries Keck, had described arranging the interview as a "challenging and bizarre experience." Public affairs officials at the EPA had told Keck that the station could not contact Titus ahead of time, and it had been unclear whether he would be available until the day before the interview.

  When asked about these hurdles on the show, Titus responded, "To be honest I don't know anything about it. I just heard about the interview and here I am." As to whether he could discuss regulating carbon dioxide, Titus replied, "I'm not allowed . . . I can't talk about what we should do as regards regulations because it's sort of a different aspect . . . Since I'm here as an EPA employee I gotta basically stick to my lane which is rising sea levels" (Titus 2006).

The Right to Publish

In the early 1990s, the EPA began to assess its requirements for internal and external peer review of its scientific work (NRC 2000; EPA Expert Panel 1992). This effort culminated in the agency's 1998 *Peer Review Handbook* (SPC 2006), an attempt to ensure quality control over the EPA's products. However, this handbook does not provide much guidance on how EPA scientists can get clearance to publish in scientific journals, and some divisions have instituted policies that unduly restrict the expression of scientific opinion:

> **Remove the political screening step in science at the Agency. For example, we are not allowed to talk to the press when they call but must refer them to a person in the front office. Often this results in the press not getting the true facts but only those that don't make the Agency look bad.**
>
> A scientist from the Office of Prevention, Pesticides and Toxic Substances

- In a law review journal, Todd Stedeford, a former EPA scientist, described the clearance process at the NCEA as "a policy of prior restraint that has escalated to censorship on publishing." He notes that the policy "appears to violate the First Amendment rights of government scientists who wish to contribute articles written outside of their official duty hours" (Stedeford 2007).

  According to Stedeford, the NCEA's clearance process is far more extensive than that outlined in the *Peer Review Handbook*. A scientific article with "policy implications" can require up to four levels of internal review before the author can submit it to a scientific journal, which would then subject it to its own peer-review process. Manuscripts submitted from the EPA's Integrated Risk Information System (IRIS) require up to seven levels of internal review (NCEA 2003). In Stedeford's experience, the agency may hold up a manuscript at any stage based on the "prejudices and whims of each reviewing official," and he reports that there is no consistency between various stages of review:

"The author has first-hand experience of the inefficiency and disorganization of this system. A manuscript that he co-authored and submitted for clearance in February of 2006 (intended for a peer-reviewed scientific journal) was still in clearance as of July 19, 2006. Several sections were required to be removed during the first-round of clearance review that were later identified as necessary elements by subsequent reviewers. After repeated complaints by the authors about the management's timely review, the management stated on July 20, 2006, that the paper had policy implications. Since this time, two of the EPA co-authors requested that their names be removed from the manuscript. Further, the corresponding author of that manuscript, Dr. Ching-Hung Hsu, has since left the Agency because of the draconian restrictions placed on publishing" (Stedeford 2007).

More disturbingly, Stedeford says he was required to submit articles written on personal time for EPA clearance:

"The author was told that if he wanted to submit a manuscript to a law review that included a brief biographical sketch, including past and present employment, education, etc., he was required to send the article through clearance. Alternatively, he was told that he could submit the article to a law review if he removed any mention of EPA, despite the fact that a prominent disclaimer was to be placed on the cover page and that the manuscript was written outside of his duty hours" (Stedeford 2007).

Dr. Stedeford left the EPA shortly after the ~~publication of the law review~~ article.

- In an interview with UCS, another EPA scientist (who asked to remain anonymous) also described problems with getting clearance to publish in scientific journals (Anonymous EPA scientist 2008a).

- In another interview, Ami Zota, a non-EPA research scientist working on environmental health, related her experience collaborating with ORD scientists on a research project and a subsequent paper. In early 2008, Zota's EPA coauthors sent the paper through the agency's internal peer review process, which Zota said was timely, and the EPA reviewer provided helpful technical comments. However, EPA policies also required the signature of the coauthors' supervisor before clearance could be granted, and at that stage the review became nontechnical and "political" in nature.

  The paper included standard disclaimers that the findings represented the opinion of the authors and not EPA policy. The supervisor nevertheless told Zota that a handful of sentences in the discussion section were "probable red flags," and that the authors would have to send the manuscript to EPA headquarters, which could delay publication by several months. The supervisor suggested that Zota delete all references to children and children's health—topics that were not the paper's primary focus, but that follow-up investigations would address.

Zota accepted some of the supervisor's suggestions, but she felt it was her scientific prerogative to frame those topics and future research in the way she saw fit. After a few conference calls, the supervisor granted clearance without further upstream review. However, Zota called the experience "intimidating," and noted that "I now understand how nuanced efforts to censor science might occur at the EPA" (Zota 2008).

Discussion

The free exchange of ideas is a pillar of the scientific enterprise. For a robust scientific enterprise to flourish at the EPA, it must allow scientists to participate fully in the scientific community. Democratic governance also depends on ensuring that citizens have comprehensive and reliable information on their government's activities (apart from some cases involving national security). For both reasons, the EPA must allow its scientists to communicate their findings in scientific publications, at scientific conferences, and to the media and the public.

Scientists do not relinquish their First Amendment rights when they become federal employees. They have a right to speak on any topic—including policy-related matters and those outside their direct field of expertise—so long as they clarify that they do so as private citizens, not as representatives of the agency or the government as a whole. Scientists should also have the right of final review of any agency product that draws on their work, to ensure that scientific information remains accurate after review, editing, and clearance.

Internal peer review of scientific publications can greatly improve the quality of EPA science. Indeed, because government agencies have a responsibility to provide high-quality scientific information to the public, we can expect a greater level of review at the EPA than in academia or the private sector. The EPA also has a legitimate interest in speaking with one voice on official policy. However, political review of scientific publications for the merest hint of a policy implication can cross the line into censorship of legitimate scientific opinion. Excessive, protracted, and confusing clearance policies both undermine the quality of agency science and harm the EPA's scientific reputation.

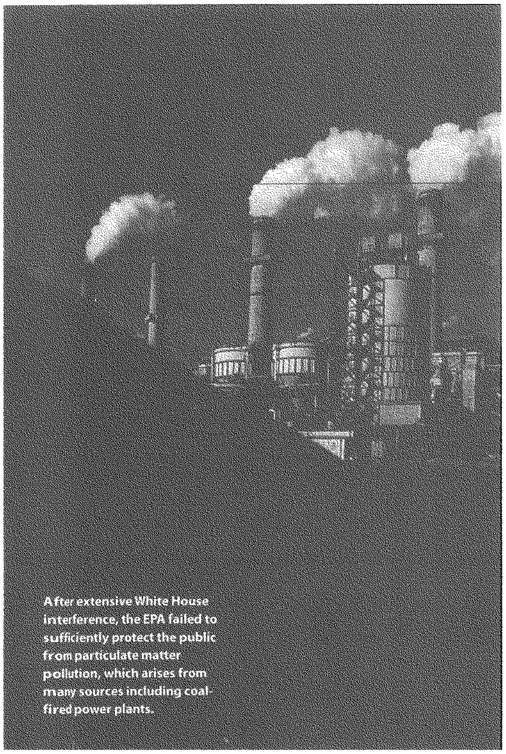
Caveats might apply to these principles that might not apply at a nonregulatory agency, such as restrictions on topics under litigation. However, the EPA has stated its desire to foster a strong scientific workforce, and it produces a significant body of scientific work. Thus the agency also has a responsibility to the U.S. public and its scientific workforce to ensure the free communication of science above and beyond basic principles.

Our survey results reveal a gap between official EPA rhetoric on scientific openness and the reality for career scientists trying to communicate their research findings. To bridge this gap, EPA leaders should clarify and strengthen the agency's openness policies, to bring them into line with basic scientific freedoms. Congress and the next president should also empower EPA scientists—perhaps through whistle-blower protections—to voice dissenting scientific opinions both internally and in the media.

CHAPTER 6

Undermining the Role of Science in EPA Decision Making

Scientific information is the lifeblood of much of the EPA's work, and the credibility of its decisions depends on the quality of its scientific work. While science is often not the only ingredient in policy making, many EPA scientists feel the agency could more effectively and consistently use both internal and external scientific expertise.



After extensive White House interference, the EPA failed to sufficiently protect the public from particulate matter pollution, which arises from many sources including coal-fired power plants.

Furthermore, the process for setting air pollution standards has become heavily politicized despite a clear legislative mandate that science be the sole criterion for setting those standards. The EPA has also attempted to institutionalize policies that marginalize scientific assessments of the health effects of air pollutants in setting future air quality standards. And the EPA has allowed members of scientific advisory committees with conflicts of interest to influence proposed regulation of contaminated groundwater.

Survey Results

Our survey asked respondents about the relationship between the EPA's scientific determinations and its policy decisions. While a plurality of EPA scientists reported that EPA policies are often consistent with the agency's scientific findings, a similar number felt that the EPA could do a better job of relying on the best judgment of its scientific staff:

- 640 scientists (42 percent) felt that the EPA's determinations frequently or always make use of the best judgment of its scientific staff. However, 719 scientists (47 percent) felt that the agency's determinations occasionally, seldom, or never do so. A total of 182 scientists (12 percent) did not know.
- 745 scientists (48 percent) felt that EPA determinations are frequently or always consistent with the scientific findings in agency documents. However, 565 scientists (37 percent) felt that this was occasionally, seldom, or never true, while 229 (15 percent) did not know.

Hundreds of EPA scientists also felt that the agency only occasionally incorporates expert advice from advisory committees into its policy decisions:

- 615 scientists (40 percent) felt that the agency frequently or always incorporates expert advice from independent scientific advisory committees into regulatory decisions. However, 553 scientists (36 percent) felt that the agency occasionally, seldom, or never heeds such advice.

- The results were markedly worse among scientists at the Office of Air Quality Planning and Standards, which works closely with the external Clean Air Scientific Advisory Committee to set the National Ambient Air Quality Standards (see below). Half of these respondents (29 scientists, or 50 percent) felt that the agency heeded the advice of advisory committees occasionally or less often.

Case Studies

Politicizing Air Quality

As Chapter 2 noted, the Clean Air Act requires the EPA to set National Ambient Air Quality Standards (NAAQS) for six "criteria" air pollutants (ozone, fine and coarse particulate matter, lead, nitrogen dioxide, sulfur oxides, and carbon monoxide), and to review each standard every five years. These standards have been a pillar of widespread improvements in air quality and public health.

Under the act, the EPA must base the NAAQS on the "best available science." In 2001 the Supreme Court confirmed that the agency cannot consider costs and other factors in setting the NAAQS (*Whitman v. American Trucking Associations, Inc.* 2001). However, Administrator Johnson has recently overruled the consensus view of EPA scientific staff and the recommendations of the Clean Air Science Advisory Committee (CASAC) by setting or proposing standards for fine particulate matter, lead, and ozone not based on the best science, and not sufficiently protective of public health. Even more troubling, the EPA has attempted to cut science out of the standard-setting process:

- Fine particulate matter (or $PM_{2.5}$) consists of particles less than 2.5 micrometers in diameter. More than 2,000 peer-reviewed studies link $PM_{2.5}$ pollution to strokes, heart disease, respiratory ailments, and premature death (American Lung Association 2005).

Science and technical information needs to be given more weight in decision-making rather than just seen as background information.

A scientist from an EPA regional office

A 2005 EPA risk assessment found that $PM_{2.5}$ pollution causes more than 4,700 premature deaths each year in just nine cities (EPA 2005), while other studies have estimated that tens of thousands of people die nationwide each year from $PM_{2.5}$ exposure (Abt 2000). Based on its review of the scientific evidence, CASAC ~~recommended tightening the yearly average~~ standard for $PM_{2.5}$ from 15 micrograms per cubic meter to 13–14 micrograms per cubic meter. Yet Administrator Johnson issued a final rule in September 2006 that left the standard unchanged.

No EPA administrator had disregarded CASAC's advice in its nearly 30-year history. Yet Johnson claimed that CASAC's nearly unanimous 22 to 2 vote was evidence of disagreement on the science. Shortly after the EPA announced the final rule, CASAC members voiced their objections in a letter to Johnson, emphasizing that, "There is clear and convincing scientific evidence that significant adverse human-health effects occur" at the new $PM_{2.5}$ standard, and that it "does not provide an 'adequate margin of safety . . . requisite to protect the public health' (as required by the Clean Air Act)" (CASAC 2006a).

CASAC members also alleged that the EPA had "twisted" or "misrepresented" the panel's recommendations on a number of issues related to the proposed standards. Bart Ostro, chief air pollution epidemiologist at the California EPA, charged that "the EPA had incorporated 'last-minute opinions and edits' by the White House Office of Management and Budget that 'circumvented the entire peer review process.'" Ostro also pointed out that the White House's changes were "very close to some of the letters written by some of the trade associations" (Wilson 2006).

- The White House also directly intervened in the EPA's recent decision regarding the primary and secondary NAAQS for ozone. Ground-level ozone—a component of smog—is created by chemical reactions between oxides of nitrogen and volatile organic compounds in the presence of sunlight. Multiple studies have shown that exposure to ozone pollution can cause and exacerbate a variety of respiratory health problems, and can even lead to premature death (Shprentz 2007).

> **Managers need to learn to trust the expertise of the technical staff.**
>
> A scientist from the Office of Water

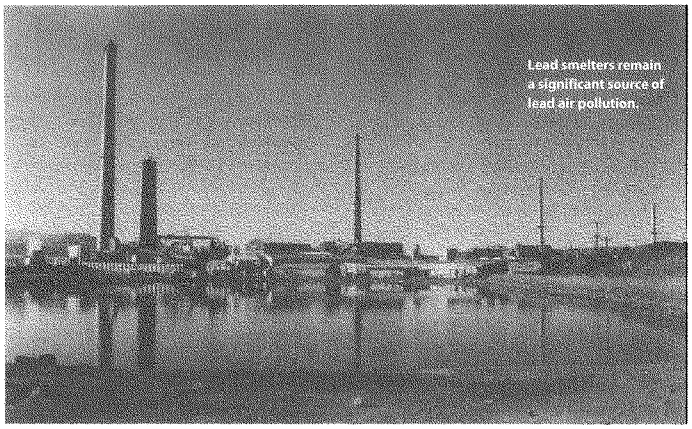
CASAC unanimously recommended tightening the ozone standard from 80 parts per billion (ppb) to a level as strict as 60 ppb, and in no case higher than 70 ppb. To support that standard, the committee cited recent controlled clinical studies documenting "statistically-significant decrements in lung function" at concentrations of 80 ppb, and "adverse lung function effects" in some individuals at 60 ppb (CASAC 2006b).

Industry groups and local governments actively lobbied both the White House and the EPA to maintain the 80 ppb standard (Boyle 2008). The OMB also manipulated the EPA's regulatory impact assessment to cast doubt on the health benefits of a lower standard (see Box 1, p. 28) (OMB Watch 2007; Patton 2007).

On March 12, 2008, Administrator Johnson again overruled CASAC to set the primary NAAQS for ozone at 75 ppb—a level unsupported by the best available science (EPA 2008). Johnson also called for changing the Clean Air Act to allow the EPA to consider the costs of complying with the standards when setting the NAAQS—a move that drew immediate condemnation from Congress (Eilperin 2008).

President Bush also personally intervened to prevent the EPA from adopting a stronger secondary standard for ozone. The Clean Air Act allows the EPA to set secondary standards to protect the "public welfare"—a broad term that includes lower visibility, ecological damage, and other concerns—beyond the primary standards designed to protect public health. The EPA often sets secondary NAAQS that are identical to the primary standards. However, the agency proposed a more stringent seasonal standard for ozone, to protect crops and other plant life during times of intense exposure.

A March 6, 2008, memorandum from OIRA head Susan Dudley to Administrator Johnson questioned the EPA's scientific basis for the secondary standard, and called on the agency to consider "economic values, personal comfort and well-being" (Dudley 2008). EPA Deputy Administrator Marcus Peacock replied that the EPA was barred by law from considering economic costs, and that the EPA was unaware of "any information indicating beneficial effects of ozone on public welfare" (Peacock 2008). Confidential talking points prepared for Administrator Johnson's March 11 meeting with President Bush also emphasized strong scientific support for the EPA's proposal (Johnson 2008).



Lead smelters remain a significant source of lead air pollution.

Despite this pushback from the EPA, a last-minute intervention by President Bush over~~ruled the agency's proposal and established~~ a secondary standard identical to the primary one. The *Washington Post* reported that Solicitor General Paul Clement warned that Bush's decision contradicted the agency's past submissions to the Supreme Court defending against industry challenges, and touched off a "scramble" to create new legal justifications for the weakened secondary standard (Eilperin 2008b).

- In December 2006, after the controversy surrounding the $PM_{2.5}$ decision, Deputy Administrator Peacock announced a new streamlined policy for setting the NAAQS that removes independent assessments by scientific experts and injects political determinations much earlier in the decision-making process (Peacock 2006).

For decades, the foundation of the NAAQS process was the staff paper, a comprehensive overview of the health effects of the air pollutant in question by EPA scientists. Staff scientists also worked with CASAC to review the latest studies and recommend appropriate standards. Only after this scientific review ~~was complete would the administrator~~ create a draft standard.

The new rules for setting the NAAQS eliminate this critical independent scientific assessment. High-level political appointees are involved right from the start, working with staff scientists to create a document containing "policy-relevant science" that "reflects the agency's views." CASAC is cut out of the process until after the EPA has announced its proposed standard, when the advisory group can comment just like any other member of the public. The new rules closely follow recent recommendations from the American Petroleum Institute (Boxer et al. 2006).

- The first criteria pollutant to be reviewed under these new rules is lead, a powerful neurotoxin that accumulates in human and animal tissue. Even low levels of lead can cause osteoporosis, high blood pressure, heart disease, anemia, memory problems, and seizures in adults. Children are at the greatest risk: even low levels of lead can lower IQ levels and cause learning deficits (AAP 2005; Lanphear et al. 2005). Regulation of lead under the Clean Air Act has dramatically reduced levels in the air and people's blood—one of the crowning public health achievements of the past 30 years.

The severing of independent scientific assessment from the policy-making process is evident in the recent Advanced Notice of Proposed Rulemaking (ANPRM) for lead. Despite scientific consensus on the value of a strong lead standard, the ANPRM seeks input on policy options that would result in a weaker lead standard and even considers removing lead from the criteria pollutant list entirely—options that CASAC explicitly rejected (EPA 2007).

CASAC members strongly criticized the ANPRM for lead at a December 2007 meeting. According to one member, "This comes ~~across as an attempt to mystify the process~~ so EPA can come up with whatever [standard] it wants." Another asserted that the process "questions the legitimacy of CASAC's mission." The advisory group plans to propose significant changes to the process by which the EPA sets the NAAQS (Inside EPA 2007c). A final decision on the lead NAAQS is expected sometime in 2008.

Conflicts of Interest and Oil Extraction

Another example of the EPA's misuse of scientific expertise relates to domestic oil extraction, and the exposure—by an EPA whistle-blower—of conflicts of interest among the agency's independent advisory committees.

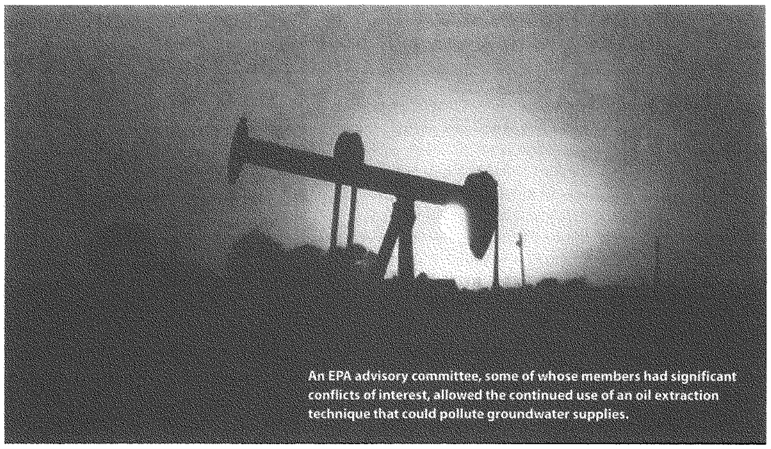
Hydraulic fracturing is a controversial technique, developed by Halliburton, that increases the amount of oil extracted from a well by pumping water or another fluid into rock under such high pressure that it creates new cracks around an oil reservoir. Critics contend that hydraulic fracturing should be regulated because toxic fluids pumped into the ground during fracturing may seep into groundwater. The oil industry has steadily maintained that the practice is safe (Hamburger and Miller 2004b).

The EPA launched a study in response to a 1994 petition from Alabama residents claiming that the process had contaminated their drinking water, and to a 1997 court ruling that hydraulic fracturing should be regulated under the Safe Drinking Water Act. However, a 2001 report from Vice President Cheney's energy task force touted the benefits of hydraulic fracturing while ignoring its potential consequences, despite repeated requests from EPA scientists that the report mention environmental concerns (Hamburger and Miller 2004b).

In 2004 the EPA released a report concluding that hydraulic fracturing posed little threat to underground drinking water supplies, and thus did not merit further study or regulation (EPA 2004). The agency claimed that the report had ~~passed peer review by an independent panel~~ of experts. However, shortly after release of the study, Weston Wilson, an environmental engineer and 30-year EPA veteran, spoke out. In an 18-page technical analysis sent to the agency's inspector general and congressional leaders, Wilson, who sought whistle-blower protection, wrote:

> "EPA's conclusions are unsupportable. EPA has conducted limited research reaching the unsupported conclusion that this industry practice needs no further study at this time. EPA decisions were supported by a Peer Review Panel; however five of the seven members of this panel appear to have conflicts-of-interest and may benefit from EPA's decision not to conduct further investigation or impose regulatory conditions" (Wilson 2004).

"I think the agency's acted egregiously," Wilson said in a later interview. "It's not fulfilling its responsibility to protect public health" (Hartman 2005).



An EPA advisory committee, some of whose members had significant conflicts of interest, allowed the continued use of an oil extraction technique that could pollute groundwater supplies.

Discussion

Our survey responses indicate serious systemic problems in how the EPA uses the expert advice of its staff scientists and independent advisory committees. Politicization of scientific advice—such as in the manipulation of the NAAQS process—endangers public health and also undermines the EPA's scientific reputation, just as severely as the overt political interference documented in Chapter 4.

The Clean Air Act requires the agency to base the NAAQS on the best available science to protect human health. These health-based standards have been extraordinarily successful in encouraging the use of innovative technology to control pollution, and air pollution has steadily declined across the country as a result. Recent EPA decisions on particulate matter and ozone clearly do not incorporate the best available science, and the consequences can be measured in growing numbers of hospital visits and premature deaths (Shprentz 2007; American Lung Association 2005).

Beyond cases where the EPA must rely on the best science to set standards, the agency's administrator has publicly and dramatically overruled the consensus advice of scientific and legal staff in several high-profile decisions. For example, in late December 2007, Administrator Johnson denied California the right to regulate global warming pollution under the Clean Air Act, despite the consensus opinion of EPA staff that his decision was scientifically and legally indefensible (Eilperin 2007). In a similar recent decision, lobbying by agricultural interests led the EPA to exempt farms and other agricultural facilities from reporting toxic emissions—again despite findings by staff scientists that such emissions could harm nearby residents (Williamson 2008).

The EPA administrator sometimes has the latitude to create policies that ignore scientific consensus. However, the agency should at least acknowledge its science, and provide a transparent rationale for its decisions. The perception that the agency is putting political and industrial interests ahead of public health and the consensus of its scientific staff severely damages its reputation for scientific objectivity and the morale of its experts.

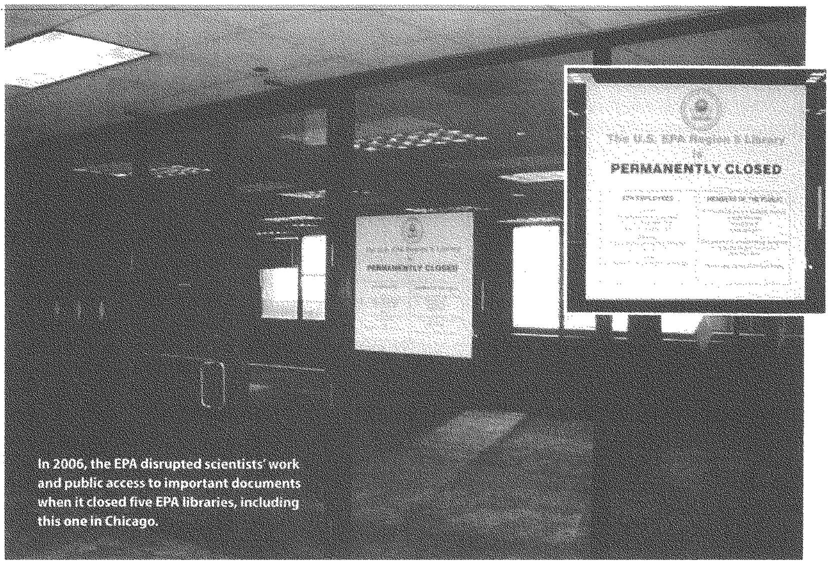
CHAPTER 7
Challenges to Agency Effectiveness

A strong EPA is essential to the health and safety of Americans. For the agency and its scientific enterprise to function effectively—that is, to ensure that it can collect the information and conduct the analyses it needs to pursue robust enforcement of environmental statutes—it must have the ability to attract and retain high-quality scientists. Several survey questions asked EPA scientists about factors beyond political interference that affect their ability to do their job, and the ability of the EPA as a whole to fulfill its mission. These factors included resources, morale, and agency effectiveness. We also examined the EPA's funding, enforcement, and monitoring.

Survey Results
Resources
Many EPA scientists indicated that a lack of sufficient or appropriate resources was a serious problem in their office or division:

- 969 scientists (62 percent) disagreed or strongly disagreed that the "EPA division where I work has sufficient resources to adequately perform its mission of protecting human health and the environment." Nearly 200 scientists also addressed this issue in their essays.

- 555 scientists (36 percent) agreed or strongly agreed that the "recent changes and closures



In 2006, the EPA disrupted scientists' work and public access to important documents when it closed five EPA libraries, including this one in Chicago.

in the EPA library system have impaired my ability to do my job." This opinion was especially prevalent among scientists in regions 5, 6 and 7, which had their libraries closed (86 of those scientists, or 48 percent, agreed). However, the impact of the closures was felt across the entire EPA.

- 574 scientists (41 percent) agreed or strongly agreed that "the trend toward contracting out scientific work is harming the effectiveness of my division." This sentiment was especially strong among scientists working in the Office of Research and Development (ORD) (198 scientists, or 52 percent).

- A clear majority of respondents (984 scientists, or 62 percent) reported that they are "provided with the appropriate time and resources to keep up with advances in my profession, including attending conferences and participation in scientific or professional ~~societies." However, 466 scientists (29 per~~cent) disagreed or strongly disagreed.

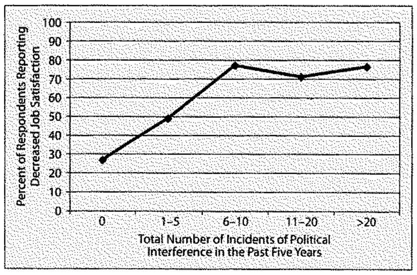
Morale and Job Satisfaction

The survey also asked scientists about their job satisfaction and the overall morale in their division:

- Twice as many respondents reported a drop in job satisfaction (670 scientists, or 44 percent) over the past five years as those who reported an increase (328 scientists, or 21 percent). Those with personal experience with political interference had a higher likelihood of declining job satisfaction (see Figure 10).

- Opinions about workforce morale varied widely. A total of 564 scientists (37 percent) said morale was fair, while another 387 scientists (25 percent) said morale was poor or extremely poor. A total of 570 scientists (37 percent) said morale was good or excellent.

FIGURE 10: **Decreased Job Satisfaction and Political Interference**



Scientists who had experienced political interference were more likely to report decreased job satisfaction.

Agency Effectiveness

Several questions addressed the overall effectiveness of the EPA. Respondents were more likely to praise the agency's accomplishments on some measures of effectiveness, while they ~~were more evenly split on other measures:~~

- Respondents were more likely to agree than disagree that the EPA was acting effectively to clean up environmental problems. A total of 812 scientists (52 percent) agreed that the EPA acts effectively to "clean up and/or mitigate existing pollution or environmental problems," while 522 scientists (33 percent) disagreed.

- The gap was narrower for preventing environmental degradation. A total of 694 scientists (44 percent) agreed that the EPA acts effectively to "foster practices that prevent environmental degradation or adverse health effects before they occur," but 629 scientists (40 percent) disagreed.

- 657 scientists (50 percent) personally experienced frequent or occasional "new or unusual administrative requirements or procedures that impair my scientific work."

- 696 scientists (45 percent) reported that the effectiveness of their division or office had declined compared with five years ago, while only 321 scientists (21 percent) said effectiveness had increased. Scientists in parts of the ORD, including the National Health and Environmental Effects Research Laboratory (NHEERL), were the most likely to report decreases in effectiveness.

> **I have never seen morale at a lower point than we currently have in EPA. Good scientists are leaving because they can no longer put up with all the micro-management that is heaped on them in lieu of effective administrative leadership.**
>
> A scientist from the Office of Research and Development

- Respondents are evenly split on whether ~~the EPA~~ is ~~moving in the right direction: 685~~ scientists (44 percent) disagreed that the EPA is moving in the right direction, while 624 (40 percent) agreed.

Case Studies

The EPA's funding has declined in real dollars over the past several years. Specific changes have also occurred that could degrade the agency's ability to conduct cutting-edge scientific research and adequately enforce the nation's environmental laws.

Library Closures

In the summer of 2006, the EPA closed large parts of its network of 27 libraries, potentially putting decades' worth of valuable information beyond the reach of government scientists, independent researchers, and the public (OEI 2006). Despite a 2004 report that found that the agency's libraries saved more than 214,000 hours a year in staff time, worth $7.5 million (OEI 2004), the Bush administration cut $2 million out of the 2007 $2.5 million library services budget, leading to the closures.

Five EPA libraries closed—the headquarters library, the chemical library of the Office of Prevention, Pesticides and Toxic Substances, and libraries in regions 5, 6, and 7—while those at several other branches reduced their hours and services. Hundreds of survey respondents noted that these closings have made it more difficult for EPA employees to do their jobs.

EPA officials claim that all materials will eventually be available online as part of a planned library modernization effort. However, many essential library holdings—from copyrighted reference books to older volumes of scientific journals—cannot be reproduced online. And the agency closed the libraries before beginning the time-consuming process of digitization, making many resources and materials unavailable indefinitely.

The closings have drawn widespread criticism from scientists, historians, the American Library ~~Association, the EPA's employee unions, and~~ others. Members of both the House and Senate called on Administrator Johnson to cease and desist with the closures (Boxer et al. 2006; Gordon et al. 2006). And a GAO report faulted the EPA for not adequately consulting library users or performing a thorough assessment of essential library services (GAO 2008). The agency has responded by promising to reopen the libraries before the end of the 2008 fiscal year (O'Neill 2008).

Enforcement and Monitoring

Weak or inconsistent enforcement can undercut even the wisest government policies. In the first five years of the Bush administration, the EPA opened fewer criminal investigations, filed fewer lawsuits, and levied smaller fines against polluters than in the final five years of the Clinton administration. The result of this drop in enforcement is that it "now costs less to pollute" (Environmental Integrity Project 2007).

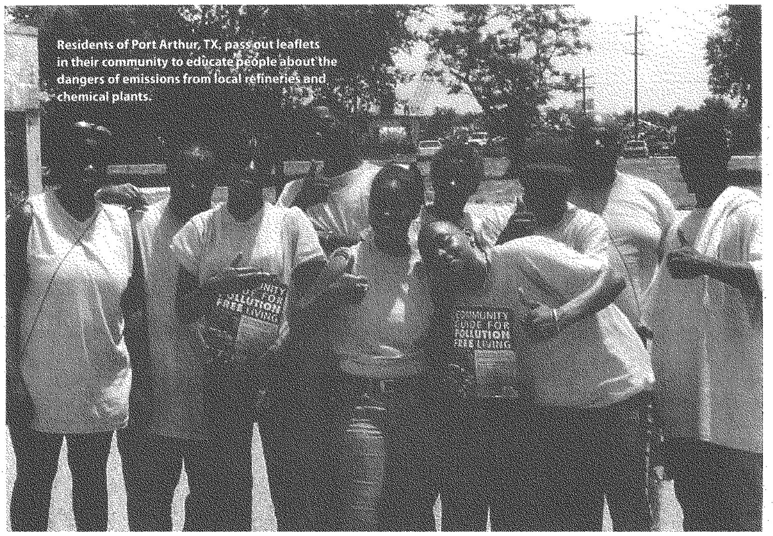
The number of criminal investigators employed by the EPA has also fallen below the minimum set by Congress (Beamish 2007). And the Bush administration has undermined EPA lawsuits already under way by weakening regulations to allow aging power plants to emit more pollution (the policy that prompted Administrator Whitman's resignation as related in Chapter 1; see Eilperin 2005).

What's more, monitoring is a crucial component of effective enforcement, and the EPA is simply not collecting essential data in many critical areas. For example, the network of sites for monitoring lead air pollution shrank from more than 900 in 1980 to little more than 200 in 2005. Today only two of the 27 worst sources of such pollution are within one mile of a monitoring site (EPA 2007). Other monitoring and reporting programs weakened under the Bush administration include the Toxics Release Inventory and the requirements for reporting agricultural emissions (see Chapter 6).

Toxics Release Inventory

The EPA's Toxics Release Inventory (TRI) requires manufacturers to provide annual reports on their use and release of more than 600 toxic chemicals. The TRI is widely credited with enhancing public knowledge and triggering significant voluntary reductions in emissions of many pollutants. Each year brings dozens of new examples of communities that have relied on the TRI to win protection from dangerous chemicals such as lead, mercury, and chromium (UCS 2006). For example, after the *Chicago Tribune* published TRI data from a local brass foundry, a citizen activist group formed and successfully negotiated protection for residents from extremely high lead levels (Hawthorne 2006).

Yet in early 2007 the EPA finalized a plan—known as the TRI burden reduction rule—to scale back reporting requirements by raising the threshold below which facilities are allowed to submit only minimal information (EPA 2006b). The rule also weakened reporting requirements for the production of persistent toxins that accumulate in plants and animals, such as mercury, lead, and PCBs. The new rule drew widespread criticism for reducing the amount of useful information that the TRI made available to the public.



Residents of Port Arthur, TX, pass out leaflets in their community to educate people about the dangers of emissions from local refineries and chemical plants.

COMMUNITY GUIDE FOR POLLUTION FREE LIVING
COMMUNITY GUIDE FOR POLLUTION FREE LIVING

A 2007 GAO investigation found that the rule disproportionately affected low-income and minority communities, and that the EPA did not conduct the required environmental justice assessment. The GAO also found that the OMB had pressured the EPA to pursue specific policy options that EPA experts had previously discarded, and set an unrealistic deadline, leading to a rushed analysis of the options. The GAO stated that the estimated savings from the rule are "likely overstated," and that the EPA's analysis "masked" the large impact the rule would have on communities across the country (GAO 2007).

MORE FUNDING! We do NOT have the resources to meet our mission. My division has seen its resources—in purchasing power—cut over 50% since 10 years ago.

A scientist from the Office of Research and Development

Discussion

Nearly half of EPA scientists who responded to our survey say their job satisfaction has declined over the past five years. Our survey cannot shed definitive light on the reasons for this decreasing job satisfaction and low morale. However, the correlation we found between political interference and lower levels of job satisfaction suggests that disrespect for the work of scientists affects their workplace environment.

Funding for the EPA's critical work has declined in real dollars since 2004. This decline in EPA resources is not itself a form of political interference as there are many national priorities that compete for scarce budget dollars. Yet funding decisions within the EPA can reflect politicization of agency priorities. These cuts, coupled with growing agency responsibilities as well as the politicization of enforcement priorities (exemplified by Administrator Whitman's resignation), can hurt staff morale even as they undermine the agency's effectiveness.

These problems make it more difficult for the EPA to attract and retain the best and brightest scientists, who are drawn by the opportunity to advance the public interest. And the strength and commitment of the agency's scientific workforce, in turn, affects its effectiveness in protecting human health and the environment.

In an interview with UCS, an anonymous EPA ~~scientist described the consequences of politi~~cal interference for staff morale and retention of top scientists, stating, "The problem is a lack of vision among the leadership. They don't look beyond the political landscape to remember the mission of the agency. This makes it hard to keep younger scientists. Your idea of what is possible diminishes, and then you leave" (Anonymous EPA scientist 2008b).

CHAPTER 8
Recommendations and Conclusions

The results of our survey and interviews with EPA scientists show widespread problems at the agency. Hundreds of scientists report direct and indirect interference with their scientific work by political appointees at the EPA and the White House. Despite claims to the contrary from EPA leaders, scientists also report institutional barriers to freely communicating their findings through both the media and scientific publications. EPA scientists are not confident that environmental decision makers respect their expertise. And the agency's effectiveness needs to improve on several fronts.

Wide-ranging political interference in EPA science requires a suite of reforms in five major ~~areas: protecting EPA scientists, improving the~~ agency's transparency, reforming its regulatory framework, strengthening its system of scientific advice, and depoliticizing funding, monitoring, and enforcement. These efforts to revitalize the EPA, allowing it to fulfill its mission of protecting human health and the environment, will require strong leadership from Congress, the next president, and the next EPA administrator, joined by EPA scientists and the broader scientific community.

Protecting EPA Scientists

To fulfill their profound responsibility to the public, EPA scientists need assurance that standing behind their scientific work will not open them to either official or unofficial retaliation. Congress is now considering several bills that would strengthen the federal whistleblower system:

- Both houses of Congress have passed legislation that would enhance protections

for whistle-blowers under the Whistleblower Protection Act of 1989, and members are now working to reconcile the two versions. The House version includes specific protections for scientists. It also defines abuse of authority to include actions that distort science, disseminate false or misleading information, and restrict scientists from publishing or speaking at conferences.

- Members of the House and Senate have introduced bills to reauthorize the Office of Special Council and the Merit Systems Protection Board—federal entities that investigate claims of reprisal against federal whistle-blowers and adjudicate whistle-blower claims, respectively. Although the legislation includes many important reforms, the Senate has taken no action, and the House bill is still in committee.

- The House has recently passed legislation to grant inspectors general (IGs) greater autonomy and immunity from coercion by the agencies they police. The Senate has reported such legislation out of committee. Both versions contain an important requirement that IG websites enable employees to anonymously report waste, fraud, and abuse. Government scientists could use this mechanism to confidentially challenge scientific misconduct. Both versions of such legislation also give IGs subpoena power.

Congress should pass the strongest possible whistle-blower protections, and the president should sign them into law. The next EPA administrator should also work with the coalition of EPA unions to integrate the agency's Principles of Scientific Integrity (EPA 1999) into the official employee grievance procedure.

Making the EPA More Transparent

Some aspects of EPA decision making are open to public scrutiny, but many "predecisional" meetings and discussions are not. The integrity of EPA science is threatened in no small part by decisions made behind closed doors. Opening up these processes to congressional and public scrutiny is an important way to reveal and end abuses of science. The EPA should also better explain how it arrives at decisions that affect ~~health and the environment~~.

The agency should institute a transparency policy for all meetings attended by non-EPA personnel. Such a policy need not be burdensome to EPA employees: outside participants could enter the required information directly into a database before any meeting, or within a specified time period after a meeting.

- This policy should require the EPA to post all meetings with outside entities on its website, including those with for-profit and not-for-profit organizations, and representatives of other agencies.

- The database should include the names and affiliations of attendees as well as the date, time, location, and subject of each meeting, with an exception granted for cases of national security.

Official EPA reports and documents in draft form are exempt from release under the Freedom of Information Act. Abuse of this exemption—wherein documents remain in draft form indefinitely—does occur.

- To prevent abuse of the "predecisional" exemption, the next EPA administrator should adopt procedures that allow the periodic release of documents that have remained in draft form for a given length of time.

The EPA should also publish a summary statement discussing the scientific basis for any significant policy, guidance, or regulation informed by science. This statement should be available in a timely fashion, and should include:

- The scientific rationale for a decision, and all scientific documents and data used to make it (including reasonable release of information from industry).
- A minority report voicing any significant dissenting scientific evidence or opinions.
- An explanation of how the agency resolved such differences of opinion.
- Identification by name of each official and employee who participated in the decision.

The Food and Drug Administration Amendments Act of 2007 already incorporates such transparency requirements, and the EPA could adapt them.

Reforming Media Policy

Both science and democracy thrive in an open environment. The EPA should clarify its policies on the interaction between scientists and the media to ensure that the public has access to taxpayer-funded information that affects their health and safety, and to ensure that scientists and other employees can exercise their rights to free speech:

- Any EPA media policy must respect at least two fundamental rights: (1) scientists have the right to speak freely about any topic (including EPA policy) if they clarify that they are speaking as private citizens, not as agency representatives; and (2) scientists should have the right to review and correct any official document (such as a press release or report) that cites or references their scientific work, to ensure that accuracy has been maintained after the clearance and editing process.
- Congress or the EPA may need to impose narrow restrictions on these basic rights in certain instances, such as in cases under litigation. Officials should clearly define these situations.

Strong, independent oversight and protection of "whistleblowers" (real protection—not what is there now) could stem the most damaging practices.

A scientist from the Office of Research and Development

- However, because the EPA is also a scientific agency, it should also supplement these basic rights by creating a public affairs system that actively disseminates agency research and codifies the positive rights of EPA scientists.
- The next EPA administrator should review the written policies of all offices and regions on the interaction between agency scientists and the media. Policies that do not explicitly protect scientists' fundamental right to freely communicate their scientific findings should be rewritten, and offices and regions without explicit policies should create them.
- The EPA should hold training sessions to clearly explain employees' rights in communicating their research to the media and the public, and the resources available to them to do so.

Reforming Publication Policy

Peer review is a pillar of the scientific method; political review is not. The EPA's process for clearing information for outside publication sometimes becomes a de facto policy review, and delays publication of controversial papers despite disclaimers that the views are personal.

- The next EPA administrator should review the agency's clearance policies, and work with the agency's offices and divisions to streamline excessive review.

The premise should be that all documents (except enforcement related stuff) start out as public documents unless EPA has jumped through a lot of legal hoops to be able [to] retain them.

A scientist from an EPA regional office

- A disclaimer on a published paper that it is not official agency policy should exempt it from a full policy review.
- The clearance process should set reasonable yet strict time limits on how long the agency can delay publication of a paper. If officials do not reach a decision within that time frame, the paper should automatically proceed to publication with a written disclaimer. If officials deny clearance, they should provide a written explanation to the authors.
- The process for reviewing and clearing papers for outside publication must be transparent, and thus posted on the website of each EPA office and division.

Reforming the Regulatory Process

While the White House oversees federal agencies, it must strike a balance between administration priorities and agency independence. The EPA was created to implement and enforce the nation's environmental laws, and it has developed the expertise, experience, processes, and policies to fulfill those critical duties. The regulatory process should respect the agency's reservoir of scientific and technical knowledge. Congress should also consider ways to strengthen our nation's environmental regulatory system, to fortify the EPA's scientific mission and meet the pressing challenges of the twenty-first century.

Ensuring Agency Independence

The EPA is the nation's first line of defense against threats to public health and the environment. As such, the EPA should be empowered to take the lead on environmental concerns and to push back against interference in its science and decisions by the OMB and other federal agencies. To accomplish this:

- The next president should elevate the EPA to a cabinet-level agency, or establish a Department of the Environment.
- ~~The next president should reverse executive~~ order 13422, removing the power of presidential appointees (who are unaccountable to Congress) to commence rulemaking, and returning that power to the EPA and its administrator.

The OMB and its Office of Information and Regulatory Affairs play important roles in coordinating and overseeing the regulatory process. However, those roles should not include second-guessing or editing the science underlying EPA decisions:

- The next president should establish a regulatory process that respects the scientific and technical expertise of the EPA, and that excludes the OMB from interfering in the EPA's scientific and technical determinations.
- The next president should repeal the OMB's one-size-fits-all directives on peer review and risk assessment. The EPA should have the flexibility to choose the form of peer review best suited to its needs.

- In particular, EPA experts should prepare risk assessments and the scientific component of regulatory impact assessments without interference from the OMB.

Enacting Legislative Reforms

The dozen or so environmental laws noted in Chapter 2 have led to dramatic improvements in public health and environmental quality. Yet the challenges the nation faces today are very different from those of 30 years ago. Congress should assess the adequacy of our current environmental regulatory structure, and consider reforms to close loopholes and strengthen the EPA's ability to address pressing threats to human health and the environment. (See CPR 2007 for possible recommendations.)

To support the quality of the EPA's scientific work, these reforms should focus on ensuring that the agency has the regulatory tools it needs to collect critical environmental data. Such tools could include stronger scientific testing requirements for pesticides and chemicals used in commerce, expanded TRI reporting requirements, and the authority to broaden environmental monitoring networks where necessary.

Congress should also consider new legislation that gives the EPA a framework to address emerging challenges such as climate change, nanotechnology, and endocrine-disrupting chemicals. Environmental justice should be a guiding principle in these efforts, to ensure that the costs of pollution and the benefits of environmental protection are shared equitably among all parts of society.

Ensuring Robust Scientific Input to EPA Decision Making

The EPA should review and strengthen the ways it uses the scientific expertise of its staff and advisory committees, especially in cases where scientific input is critical or the law requires it. The agency should also tighten its conflict-of-interest restrictions.

Disclosing and Mitigating Conflicts of Interest

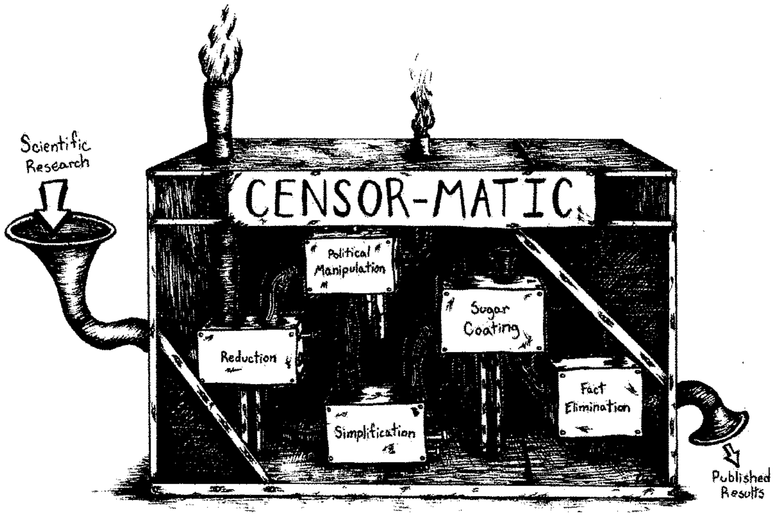
The next EPA administrator should work with employees, industry, and the scientific community to develop comprehensive conflict-of-interest policies for both staff and members of advisory committees:

- Government employees and members of advisory committees who are involved in regulation should disclose all conflicts of interest and special interests that might affect their ability to do their job in an unbiased manner.

- Individuals with a significant conflict of interest may still contribute to a project as invited experts, but the EPA should restrict them from decision making and otherwise influencing policy outcomes.

Conflict-of-interest policies should also prohibit the revolving-door practice of appointing individuals from industry as senior EPA officials responsible for regulating those industries:

- The next administration should provide clear guidelines for minimizing the appointment of senior officials with conflicts of interest.



At a minimum, federal employees should be required to recuse themselves from decisions involving former employers (RDWG 2005).

Reforming Advisory Committees

The EPA should pursue reforms to make better use of its independent advisory committees. Specifically, the next EPA administrator should work with the Clean Air Scientific Advisory Committee to improve the process for setting the National Ambient Air Quality Standards, to ensure that decision makers have access to the "best available science."

Depoliticizing Funding, Monitoring, and Enforcement

These actions are essential to restore the scientific integrity of EPA decision making. But, in addition, problems with funding, monitoring, and enforcement—which relate to the EPA's scientific integrity—also need to be addressed by Congress and the next president to ensure that the EPA is the robust environmental agency that our country needs. In particular, Congress should provide the EPA with resources commensurate with its growing responsibilities and should work to ensure that selective internal budget cuts are not used to punish inconvenient programs or offices. The next president should commit to strong and consistent enforcement of the nation's environmental laws.

Concluding Thoughts

The EPA's scientific enterprise is our nation's first line of defense against threats to public health and the environment. These threats are growing more complex and global, with the potential to harm the nation's health and prosperity. Despite notable successes, air and water pollution remain serious public health problems. Each year brings new and untested chemicals into our homes, schools, and workplaces. Climate change alone is projected to have profound impacts on public health, agriculture, the economy, and even national security.

These problems are not insurmountable. The environmental and public health successes of the past several decades show that the country can rise to the challenge of environmental threats—but only if the EPA has the proper tools. Given the complexity of today's environmental challenges, a credible scientific knowledge base is essential to an effective response. To foster and sustain a healthy scientific enterprise, Congress and the next president should take concrete steps to protect EPA scientists, make the agency more transparent, reform the regulatory process, strengthen the scientific advisory system, and depoliticize funding, monitoring, and enforcement.

Science is not the only element of effective policy making. However, because science enjoys widespread respect, appointed officials will always be tempted to manipulate or suppress scientific findings to support predetermined policies. Such manipulation is not only dishonest; it also undermines the EPA's credibility and affects the health and safety of Americans.

The science and risks and benefits need to be honestly and fairly considered. The decisions that are made should be justified and be transparent as to why a decision was made, and the risks and benefits [should] be clearly and honestly presented.

A scientist from the Office of Prevention, Pesticides, and Toxic Substances

The Bush administration's direct abuse of science—combined with systemic changes to the regulatory system that threaten the integrity of EPA science—highlight the need for strong action by the next president and Congress to restore scientific integrity to the agency's decision making. Only then can the EPA fully mobilize to serve the public good and ensure the nation's health.

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APPENDIX A

Survey Text and Responses

This appendix provides the text of the survey UCS mailed to nearly 5,500 scientists working at the U.S. Environmental Protection Agency (EPA), along with responses from the 1,586 scientists who completed and returned the surveys. The information includes two numbers for each response option: the *number* of scientists who selected that response, and the *percentage* of scientists answering the question who selected that response (in parentheses). (For a detailed analysis of select survey questions, see Appendix B.)

The total number of responses to many questions is less than 1,586 because not all respondents answered every question. For question 3, the total number of responses is greater than 1,586 because scientists could choose more than one response.

It is important to note that we calculated the percentages given here (and in the report text) based on the number of scientists answering the question, not the total number of returned surveys. Percentages for a given question may not total 100 because of rounding or multiple responses.

Respondents could include explanatory text when selecting "other" for questions 1 (major field of training), 3 (type of scientific work at the EPA), 41 (current General Schedule level), and 43 (highest level of education completed). For questions 1, 41, and 43, we used this text to reassign some of these responses to other categories. In the case of question 1, we created two new categories ("policy" and "math and economics") that did not appear as response options on the original survey.

Questions 5, 15, and 25–38 offered "not applicable" as a possible response, and we included those responses when tabulating the results here. However, we did not include those responses when analyzing results for the main text. That means that the percentages given here for those questions differ slightly from those in the main text.

We excluded respondents who reported that 0 percent of their job duties related to scientific topics (question 2).

UCS SURVEY OF EPA SCIENTISTS

Please select the best answer option for each of the following statements.

RESEARCH & TRAINING

1. My major field of training is:

Chemistry	Life Sciences	Physics	Environmental Science	Geology
164 (10.4%)	276 (17.4%)	24 (1.5%)	361 (22.8%)	102 (6.4%)

Engineering	Toxicology	Public Health	Non-Science	Other: ______
328 (20.7%)	84 (5.3%)	49 (3.1%)	66 (4.2%)	51 (3.2%)

Policy	Math & Economics
15 (0.9%)	63 (4.0%)

2. The percentage of my job duties related to scientific topics is approximately:

None	1-25%	26-50%	51-75%	76-100%
0 (0.0%)	248 (15.7%)	306 (19.4%)	436 (27.7%)	585 (37.1%)

3. My scientific work at the EPA primarily involves: (select up to two options)

Laboratory Testing	Modeling	Basic Science	Field Work
168 (10.6%)	237 (14.9%)	314 (19.8%)	202 (12.7%)

Enforcement	Compliance	Permit Writing	Risk Assessment
147 (9.3%)	184 (11.6%)	54 (3.4%)	371 (23.4%)

Oversight	Community Outreach	Program Evaluation	Grant Review
307 (19.4%)	116 (7.3%)	254 (16.0%)	106 (6.7%)

Quality Assurance	No scientific work at the EPA	Other: ______
160 (10.1%)	4 (0.3%)	345 (21.8%)

PROFESSIONAL DEVELOPMENT

4. I am provided with the appropriate time and resources to keep up with advances in my profession, including attending conferences and participation in scientific or professional societies.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
245 (15.5%)	739 (46.7%)	131 (8.3%)	364 (23.0%)	102 (6.5%)

5. I am allowed to publish work in peer-reviewed scientific journals regardless of whether it adheres to agency policies or positions.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree	Not Applicable
132 (8.4%)	350 (22.2%)	464 (29.4%)	203 (12.9%)	88 (5.6%)	341 (21.6%)

WORK ENVIRONMENT

6. I respect the integrity and professionalism of my direct manager or supervisor.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
620 (39.2%)	662 (41.8%)	108 (6.8%)	125 (7.9%)	67 (4.2%)

7. I respect the integrity and professionalism of the EPA's senior leadership.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
128 (8.1%)	558 (35.4%)	302 (19.1%)	385 (24.4%)	205 (13.0%)

8. Within the EPA I can openly express my concerns about the agency's mission-driven work without fear of retaliation.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
187 (11.9%)	658 (41.7%)	240 (15.2%)	381 (24.2%)	111 (7.0%)

9. Outside of the EPA I can openly express my concerns about the agency's mission-driven work without fear of retaliation.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
224 (14.2%)	637 (40.4%)	332 (21.1%)	288 (18.3%)	94 (6.0%)

AGENCY EFFECTIVENESS

10. The EPA is acting effectively to clean-up and/or mitigate existing pollution or environmental problems.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
126 (8.1%)	686 (44.0%)	226 (14.5%)	422 (27.1%)	100 (6.4%)

11. The EPA is acting effectively to foster practices that prevent environmental degradation or adverse health effects before they occur.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
106 (6.8%)	588 (37.7%)	237 (15.2%)	498 (31.9%)	131 (8.4%)

12. In my opinion, the EPA is moving in the right direction.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
97 (6.2%)	527 (33.8%)	252 (16.1%)	512 (32.8%)	173 (11.1%)

13. Compared to five years ago, the effectiveness of my division or office has:

Increased	Stayed the Same	Decreased	No Opinion
321 (20.6%)	389 (24.9%)	696 (44.6%)	155 (9.9%)

RESOURCES AND FUNDING

14. The EPA division where I work has sufficient resources to adequately perform its mission of protecting human health and the environment.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
61 (3.9%)	403 (25.9%)	125 (8.0%)	675 (43.3%)	294 (18.9%)

15. The trend toward contracting out scientific work is harming the effectiveness of my division.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree	Not Applicable
203 (13.1%)	371 (23.9%)	389 (25.0%)	385 (24.8%)	66 (4.2%)	141 (9.1%)

16. The recent changes and closures in the EPA library system have impaired my ability to do my job.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
154 (9.9%)	401 (25.8%)	439 (28.2%)	462 (29.7%)	101 (6.5%)

ROLE OF SCIENCE IN AGENCY DECISIONS

17. My direct supervisor consistently stands behind scientific staff or supervisors who put forth scientifically defensible positions that may be politically controversial.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
274 (17.8%)	632 (41.0%)	358 (23.2%)	209 (13.6%)	68 (4.4%)

18. EPA determinations and actions are consistent with the scientific findings contained in agency documents and reports.

Always	Frequently	Occasionally	Seldom	Never	Don't Know
58 (3.8%)	687 (44.6%)	488 (31.7%)	71 (4.6%)	6 (0.4%)	229 (14.9%)

19. Expert advice from independent scientific advisory committees is heeded and incorporated into regulatory decisions.

Always	Frequently	Occasionally	Seldom	Never	Don't Know
55 (3.6%)	560 (36.5%)	439 (28.6%)	105 (6.8%)	9 (0.6%)	368 (24.0%)

20. The EPA's determinations make use of the best judgment of its scientific staff.

Always	Frequently	Occasionally	Seldom	Never	Don't Know
77 (5.0%)	563 (36.5%)	552 (35.8%)	149 (9.7%)	18 (1.2%)	182 (11.8%)

JOB SATISFACTION

21. Over the past few years my personal job satisfaction at the EPA has:

Increased	Decreased	Stayed the Same	No Opinion
328 (21.3%)	670 (43.5%)	501 (32.6%)	40 (2.6%)

22. Morale within my division or office at the EPA is:

Excellent	Good	Fair	Poor	Extremely Poor	No Opinion
95 (6.2%)	475 (30.9%)	564 (36.7%)	259 (16.9%)	128 (8.3%)	16 (1.0%)

COMMUNICATIONS POLICIES

23. The EPA routinely provides complete and accurate information to the public.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
112 (7.3%)	651 (42.5%)	413 (26.9%)	294 (19.2%)	63 (4.1%)

24. EPA policies allow scientists to speak freely to the news media about their research findings.

Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree	Unsure
29 (1.9%)	168 (10.9%)	395 (25.7%)	492 (32.0%)	291 (18.9%)	161 (10.5%)

POLITICAL INTERFERENCE

How many cases do you know of where the following situations have occurred?

25. Cases where EPA political appointees have inappropriately involved themselves in scientific decisions.

Many	Some	Few	None	Not Applicable
150 (9.9%)	366 (24.3%)	343 (22.7%)	347 (23.0%)	302 (20.0%)

26. Cases where political appointees from other federal departments or agencies (for example, OMB, CEQ, USDA, DOD) have inappropriately involved themselves in decisions.

Many	Some	Few	None	Not Applicable
201 (13.3%)	359 (23.8%)	229 (15.2%)	356 (23.6%)	361 (24.0%)

27. Cases where commercial interests have inappropriately induced the reversal or withdrawal of EPA scientific conclusions or decisions through political intervention.

Many	Some	Few	None	Not Applicable
139 (9.3%)	368 (24.6%)	307 (20.5%)	384 (25.7%)	296 (19.8%)

28. Cases where non-governmental or advocacy groups have inappropriately induced the reversal or withdrawal of EPA scientific conclusions or decisions through political intervention.

Many	Some	Few	None	Not Applicable
57 (3.8%)	272 (18.1%)	337 (22.5%)	504 (33.6%)	329 (21.9%)

How often have you personally experienced the following situations?

29. I have been directed by EPA decision makers to provide incomplete, inaccurate, or misleading information to the public, media or elected officials.

Frequently	Occasionally	Seldom	Never	Not Applicable
15 (1.0%)	73 (4.8%)	136 (9.0%)	1117 (74.0%)	168 (11.1%)

30. EPA decision makers implicitly expect me to provide incomplete, inaccurate, or misleading information to the public, media or elected officials.

Frequently	Occasionally	Seldom	Never	Not Applicable
33 (2.2%)	90 (6.0%)	161 (10.7%)	1031 (68.4%)	193 (12.8%)

31. I have been directed to inappropriately exclude or alter technical information from an EPA scientific document.

Frequently	Occasionally	Seldom	Never	Not Applicable
23 (1.5%)	71 (4.7%)	130 (8.6%)	1119 (74.2%)	166 (11.0%)

32. Selective or incomplete use of data to justify a specific regulatory outcome.

Frequently	Occasionally	Seldom	Never	Not Applicable
71 (4.7%)	214 (14.3%)	247 (16.5%)	736 (49.1%)	232 (15.5%)

33. Pressure to ignore impacts of a regulation on sensitive populations.

Frequently	Occasionally	Seldom	Never	Not Applicable
33 (2.2%)	120 (8.0%)	158 (10.5%)	904 (60.3%)	285 (19.0%)

34. Changes or edits during review that change the meaning of scientific findings.

Frequently	Occasionally	Seldom	Never	Not Applicable
53 (3.5%)	179 (12.0%)	250 (16.7%)	787 (52.6%)	228 (15.2%)

35. Disappearance/unusual delay in the release of websites, press releases, reports or other science-based materials.

Frequently	Occasionally	Seldom	Never	Not Applicable
84 (5.6%)	215 (14.4%)	221 (14.8%)	709 (47.4%)	267 (17.8%)

36. New or unusual administrative requirements or procedures that impair my scientific work.

Frequently	Occasionally	Seldom	Never	Not Applicable
265 (17.7%)	392 (26.2%)	303 (20.3%)	361 (24.1%)	174 (11.6%)

37. Statements by EPA officials that misrepresent scientists' findings.

Frequently	Occasionally	Seldom	Never	Not Applicable
92 (6.2%)	302 (20.3%)	346 (23.2%)	511 (34.3%)	240 (16.1%)

38. Situations in which scientists have actively objected to, resigned from or removed themselves from a project because of pressure to change scientific findings.

Frequently	Occasionally	Seldom	Never	Not Applicable
29 (1.9%)	162 (10.9%)	231 (15.5%)	807 (54.2%)	259 (17.4%)

Several forms of political interference in the workplace are listed below. Most of these were addressed in the questions you have just completed (items 24–38). Please refer to the list below when answering the following two questions.

- Inappropriate influence of EPA or other agency political appointees in scientific decisions
- Inappropriate influence by commercial, non-governmental, or advocacy interests
- Directed to provide incomplete, inaccurate or misleading information to public
- Directed to exclude or alter technical information in EPA scientific document
- Selective or incomplete use of data to justify a specific regulatory outcome
- Pressure to ignore impacts of a regulation on sensitive populations
- Changes or edits during review that change the meaning of scientific findings
- Disappearance/unusual delay in the release of scientific information
- New or unusual administrative requirements that impair scientific work
- Statements by EPA officials that misrepresent scientists' findings
- Requests to consider data or use methods that are not scientifically credible
- Situations in which scientists have actively objected to pressure to change findings

39. How many activities or situations like those listed above have you personally experienced during the past 5 years?

0	1-5	6-10	11-20	more than 20
581 (39.5%)	655 (44.6%)	175 (11.9%)	34 (2.3%)	25 (1.7%)

40. If you compare the past 5 years to the 5-year period prior to it (from 5 to 10 years ago), would you say activities or situations like those listed above are occurring:

More Often than before	About the Same as before	Less Often than before	Don't Know
508 (34.4%)	330 (22.4%)	65 (4.4%)	572 (38.8%)

MY BACKGROUND

41. My current grade level is:

GS-9 or lower	GS-10	GS-11	GS-12	GS-13	GS-14
16 (1.1%)	6 (0.4%)	37 (2.5%)	138 (9.3%)	672 (45.5%)	333 (22.5%)

GS-15	SES	Other: ____________
219 (14.8%)	37 (2.5%)	19 (1.3%)

42. I have been working at the EPA for:

Less than 1 year	1-5 years	6-10 years	11-15 years	more than 15 years
21 (1.4%)	239 (16.1%)	254 (17.1%)	136 (9.2%)	833 (56.2%)

43. Highest level of education completed:

Bachelor's	Master's	PhD	JD	Other: __________
344 (23.2%)	640 (43.1%)	485 (32.7%)	10 (0.7%)	6 (0.4%)

44. How could the integrity of scientific work produced by the EPA best be improved?
855 (53.9%) respondents provided written comments in response to this question.
The full text of these essay responses is available at *http://www.ucsusa.org/surveys.*

APPENDIX B
Selected Survey Results

The tables below provide detailed data on responses to survey questions referenced in the main text. The first set of tables shows the total number of responses to the questions, broken down by offices or locations within the EPA. The second set of tables provides cross-comparisons between two survey questions. Additional survey data and analyses are available online at *http://www.ucsusa.org/surveys*.

Selected Responses by Office and Location

These tables break down survey questions based on respondents' office or location within the EPA. The leftmost column lists the response options for the given question. The column labeled "EPA total" lists the total number of respondents who ~~chose each available option. The row labeled~~ "total" lists the number of respondents answering the question, and the total respondents from each office or location.

The breakdown into individual offices and locations for each question is not complete because of the large number of EPA offices and locations. For simplicity, we analyze only the results for offices or locations specifically mentioned in the main text. The values in the right-hand columns therefore do not add up to the value in the "EPA total" column. The one exception is the breakdown for question 39, which includes all responses to that question.

The percentages in each table are based on the total number of scientists from each office or location who answered each question.

Cross-Comparisons of Selected Responses

These tables compare responses to two survey questions. The two columns on the left side list the first survey question, the available responses, and the total number of scientists who chose each option. The columns on the right side list the second survey question, the available responses, and the total number of respondents who chose each option. The row labeled "total" provides the total number of respondents on the first question, and the total number of respondents for each option on the second question. The totals for the first question will not always equal the sum of respondents for the second question because a given respondent may not have answered both questions.

Acronyms

NCEA	National Center for Environmental Assessment
NRMRL	National Risk Management ~~Research Laboratory~~
NERL	National Exposure Research Laboratory
NHEERL	National Health and Environmental Effects Research Laboratory
ORD	Office of Research and Development
OAR	Office of Air and Radiation
Water	Office of Water
OSWER	Office of Solid Waste and Emergency Response
OPPTS	Office of Prevention, Pesticides and Toxic Substances
OAQPS	Office of Air Quality Planning and Standards (OAR)
Program Offices	Combined responses from OAR, Water, OSWER and OPPTS
Admin	Office of the Administrator
HQ	EPA Headquarters in Washington, DC
RTP	EPA facilities at Research Triangle Park, North Carolina
Cincinnati	EPA facilities at Cincinnati, Ohio

QUESTION 5: **I am allowed to publish work in peer-reviewed scientific journals regardless of whether it adheres to agency policies or positions.**

		ORD Labs & Centers							
	EPA Total	NCEA	NRMRL	NERL	NHEERL	ORD Total	Program Offices	HQ Total	Regions Total
Strongly Agree	132 8.4%	2 3.9%	10 12.3%	12 14.3%	33 24.3%	62 14.9%	34 6.3%	43 7.2%	28 5.1%
Agree	350 22.2%	18 35.3%	35 43.2%	27 32.1%	52 38.2%	148 35.5%	101 18.8%	120 20.0%	83 15.0%
No Opinion	464 29.4%	7 13.7%	16 19.8%	21 25.0%	25 18.4%	84 20.1%	172 32.0%	185 30.8%	191 34.5%
Disagree	203 12.9%	22 43.1%	12 14.8%	17 20.2%	13 9.6%	79 18.9%	65 12.1%	80 13.3%	52 9.4%
Strongly Disagree	88 5.6%	2 3.9%	6 7.4%	4 4.8%	5 3.7%	22 5.3%	39 7.3%	40 6.7%	24 4.3%
Not Applicable	341 21.6%	0 0.0%	2 2.5%	3 3.6%	8 5.9%	22 5.3%	126 23.5%	133 22.1%	176 31.8%
Total	1578	51	81	84	136	417	537	601	554

QUESTION 13: **Compared to five years ago, the effectiveness of my division or office has:**

		ORD Labs & Centers				Program Offices				
	EPA Total	NCEA	NRMRL	NERL	NHEERL	OAR	Water	OSWER	OPPTS	Regions Total
Increased	321 20.6%	9 18.0%	15 18.5%	19 22.9%	17 12.8%	32 21.8%	6 6.5%	9 13.4%	79 35.6%	108 19.6%
Stayed the Same	389 24.9%	8 16.0%	13 16.1%	15 18.1%	27 20.3%	44 29.9%	23 24.7%	18 26.9%	60 27.0%	148 26.8%
Decreased	696 44.6%	27 54.0%	47 58.0%	33 39.8%	77 57.9%	56 38.1%	41 44.1%	33 49.3%	64 28.8%	262 47.5%
No Opinion	155 9.9%	6 12.0%	6 7.4%	16 19.3%	12 9.0%	15 10.2%	23 24.7%	7 10.4%	19 8.6%	34 6.2%
Total	1561	50	81	83	133	147	93	67	222	552

QUESTION 14: **The EPA division where I work has sufficient resources to adequately perform its mission of protecting human health and the environment.**

		ORD Labs & Centers				Program Offices				
	EPA Total	NCEA	NRMRL	NERL	NHEERL	OAR	Water	OSWER	OPPTS	Regions Total
Strongly Agree	61 3.9%	2 4.0%	2 2.5%	5 6.0%	3 2.3%	8 5.5%	1 1.1%	0 0.0%	11 5.0%	16 2.9%
Agree	403 25.9%	25 50.0%	15 18.8%	19 22.9%	26 19.7%	33 22.6%	33 35.1%	10 14.9%	83 37.6%	122 22.1%
No Opinion	125 8.0%	5 10.0%	2 2.5%	9 10.8%	9 6.8%	17 11.6%	6 6.4%	6 9.0%	16 7.2%	42 7.6%
Disagree	675 43.3%	12 24.0%	34 42.5%	40 48.2%	66 50.0%	66 45.2%	40 42.6%	32 47.8%	76 34.4%	260 47.0%
Strongly Disagree	294 18.9%	6 12.0%	27 33.8%	10 12.1%	28 21.2%	22 15.1%	14 14.9%	19 28.4%	35 15.8%	113 20.4%
Total	1558	50	80	83	132	146	94	67	221	553

QUESTION 15: **The trend toward contracting out scientific work is harming the effectiveness of my division.**

			ORD Labs & Centers						
	EPA Total	ORD Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Strongly Agree	203 13.1%	75 18.3%	5 10.0%	24 29.6%	14 16.9%	25 18.9%	63 11.9%	61 10.4%	61 11.1%
Agree	371 23.9%	123 30.1%	15 30.0%	24 29.6%	27 32.5%	46 34.8%	104 19.7%	111 18.8%	131 23.9%
No Opinion	389 25.0%	69 16.9%	8 16.0%	13 16.1%	18 21.7%	22 16.7%	127 24.1%	146 24.8%	170 31.0%
Disagree	385 24.8%	92 22.5%	17 34.0%	13 16.1%	14 16.9%	26 19.7%	170 32.2%	184 31.2%	106 19.3%
Strongly Disagree	66 4.2%	21 5.1%	4 8.0%	5 6.2%	4 4.8%	3 2.3%	28 5.3%	34 5.8%	16 2.9%
Not Applicable	141 9.1%	29 7.1%	1 2.0%	2 2.5%	6 7.2%	10 7.6%	36 6.8%	53 9.0%	65 11.8%
Total	1555	409	50	81	83	132	528	589	549

QUESTION 16: **The recent changes and closures in the EPA library system have impaired my ability to do my job.**

	EPA Total	Regions 5, 6 & 7	All Other Regions	HQ OPPTS	HQ Total	ORD Total	Program Offices	RTP Total	Cinn. Total
Strongly Agree	154 9.9%	19 10.6%	34 9.1%	24 10.9%	63 10.7%	46 11.2%	44 8.3%	5 2.9%	23 22.1%
Agree	401 25.8%	67 37.4%	111 29.8%	46 20.9%	139 23.6%	93 22.7%	112 21.3%	30 17.1%	23 22.1%
No Opinion	439 28.2%	34 19.0%	113 30.3%	67 30.5%	176 29.9%	102 24.9%	170 32.3%	50 28.6%	20 19.2%
Disagree	462 29.7%	49 27.4%	99 26.5%	63 28.6%	163 27.7%	143 35.0%	157 29.8%	77 44.0%	31 29.8%
Strongly Disagree	101 6.5%	10 5.6%	16 4.3%	20 9.1%	47 8.0%	25 6.1%	44 8.3%	13 7.4%	7 6.7%
Total	1557	179	373	220	588	409	527	175	104

QUESTION 19: **Expert advice from independent scientific advisory committees is heeded and incorporated into regulatory decisions.**

	EPA Total	ORD Total	RTP OAQPS	Program Offices	HQ Total	Regions Total
Always	55 3.6%	12 3.0%	0 0.0%	30 5.8%	35 6.0%	11 2.0%
Frequently	560 36.5%	144 35.9%	20 34.5%	229 44.0%	250 43.0%	163 29.9%
Occasionally	439 28.6%	112 27.9%	25 43.1%	129 24.8%	151 25.9%	174 31.9%
Seldom	105 6.8%	25 6.2%	4 6.9%	30 5.8%	34 5.8%	43 7.9%
Never	9 0.6%	2 0.5%	0 0.0%	5 1.0%	5 0.9%	2 0.4%
Don't Know	368 24.0%	106 26.4%	9 15.5%	98 18.8%	107 18.4%	152 27.9%
Total	1536	401	58	521	582	545

QUESTION 24: **EPA policies allow scientists to speak freely to the news media about their research findings.**

		ORD Labs & Centers							
	EPA Total	NCEA	NRMRL	NERL	NHEERL	ORD Total	Program Offices	HQ Total	Regions Total
Strongly Agree	29 1.9%	0 0.0%	0 0.0%	0 0.0%	2 1.6%	8 2.0%	9 1.7%	10 1.7%	11 2.0%
Agree	168 10.9%	2 4.0%	6 7.7%	7 8.6%	14 10.9%	40 10.0%	48 9.2%	55 9.5%	75 13.8%
No Opinion	395 25.7%	7 14.0%	13 16.7%	13 16.1%	17 13.2%	60 15.0%	146 28.0%	155 26.6%	169 31.0%
Disagree	492 32.0%	22 44.0%	34 43.6%	31 38.3%	55 42.6%	160 39.9%	154 29.6%	181 31.1%	155 28.4%
Strongly Disagree	291 18.9%	17 34.0%	23 29.5%	25 30.9%	29 22.5%	107 26.7%	101 19.4%	111 19.1%	74 13.6%
Unsure	161 10.5%	2 4.0%	2 2.6%	5 6.2%	12 9.3%	26 6.5%	63 12.1%	70 12.0%	61 11.2%
Total	1536	50	78	81	129	401	521	582	545

QUESTION 31: **I have been directed to inappropriately exclude or alter technical information from an EPA scientific document.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	23 1.5%	3 6.0%	1 1.3%	0 0.0%	0 0.0%	16 3.1%	16 2.8%	2 0.4%
Occasionally	71 4.7%	5 10.0%	3 3.9%	4 5.1%	6 4.6%	29 5.7%	35 6.2%	18 3.4%
Seldom	130 8.6%	9 18.0%	8 10.4%	1 1.3%	6 4.6%	60 11.8%	63 11.1%	36 6.7%
Never	1119 74.2%	29 58.0%	57 74.0%	64 81.0%	106 81.5%	351 68.8%	392 68.9%	419 78.5%
Not Applicable	166 11.0%	4 8.0%	8 10.4%	10 12.7%	12 9.2%	54 10.6%	63 11.1%	59 11.0%
Total	1509	50	77	79	130	510	569	534

QUESTION 32: **Selective or incomplete use of data to justify a specific regulatory outcome.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	71 4.7%	2 4.0%	0 0.0%	3 3.8%	0 0.0%	40 7.9%	41 7.3%	19 3.6%
Occasionally	214 14.3%	8 16.0%	5 6.6%	9 11.5%	9 7.0%	86 17.0%	100 17.7%	66 12.4%
Seldom	247 16.5%	14 28.0%	10 13.2%	3 3.8%	8 6.2%	108 21.3%	110 19.5%	84 15.8%
Never	736 49.1%	17 34.0%	46 60.5%	44 56.4%	75 58.1%	213 42.0%	243 43.1%	287 53.9%
Not Applicable	232 15.5%	9 18.0%	15 19.7%	19 24.4%	37 28.7%	60 11.8%	70 12.4%	76 14.3%
Total	1500	50	76	78	129	507	564	532

QUESTION 33: **Pressure to ignore impacts of a regulation on sensitive populations.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	33 2.2%	3 6.0%	0 0.0%	2 2.6%	1 0.8%	14 2.8%	17 3.0%	10 1.9%
Occasionally	120 8.0%	5 10.0%	2 2.6%	2 2.6%	2 1.6%	49 9.6%	62 11.0%	44 8.3%
Seldom	158 10.5%	3 6.0%	4 5.3%	5 6.4%	3 2.3%	80 15.7%	74 13.1%	54 10.2%
Never	904 60.3%	30 60.0%	54 71.1%	47 60.3%	84 65.6%	277 54.4%	319 56.4%	334 62.9%
Not Applicable	285 19.0%	9 18.0%	16 21.1%	22 28.2%	38 29.7%	89 17.5%	94 16.6%	89 16.8%
Total	1500	50	76	78	128	509	566	531

QUESTION 34: **Changes or edits during review that change the meaning of scientific findings.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	53 3.5%	7 14.3%	1 1.3%	2 2.6%	0 0.0%	27 5.3%	37 6.6%	8 1.5%
Occasionally	179 12.0%	6 12.2%	5 6.6%	4 5.1%	6 4.7%	87 17.2%	93 16.5%	52 9.8%
Seldom	250 16.7%	12 24.5%	12 15.8%	14 17.9%	13 10.1%	109 21.5%	114 20.2%	70 13.2%
Never	787 52.6%	22 44.9%	48 63.2%	45 57.7%	86 66.7%	229 45.3%	260 46.1%	296 55.8%
Not Applicable	228 15.2%	2 4.1%	10 13.2%	13 16.7%	24 18.6%	54 10.7%	60 10.6%	104 19.6%
Total	1497	49	76	78	129	506	564	530

QUESTION 35: **Disappearance/unusual delay in the release of websites, press releases, reports or other science-based materials.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	84 5.6%	15 30.0%	2 2.6%	8 10.3%	4 3.1%	36 7.1%	45 8.0%	14 2.6%
Occasionally	215 14.4%	8 16.0%	11 14.5%	12 15.4%	13 10.2%	73 14.4%	85 15.1%	74 14.0%
Seldom	221 14.8%	7 14.0%	14 18.4%	5 6.4%	8 6.3%	94 18.6%	97 17.2%	78 14.7%
Never	709 47.4%	14 28.0%	40 52.6%	36 46.2%	74 57.8%	215 42.5%	240 42.6%	270 50.9%
Not Applicable	267 17.8%	6 12.0%	9 11.8%	17 21.8%	29 22.7%	88 17.4%	96 17.1%	94 17.7%
Total	1496	50	76	78	128	506	563	530

QUESTION 37: **Statements by EPA officials that misrepresent scientists' findings.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	92 6.2%	4 8.0%	4 5.2%	7 9.0%	7 5.5%	35 7.0%	38 6.8%	28 5.3%
Occasionally	302 20.3%	18 36.0%	14 18.2%	11 14.1%	23 18.0%	109 21.7%	128 22.8%	100 19.0%
Seldom	346 23.2%	15 30.0%	17 22.1%	16 20.5%	20 15.6%	115 22.9%	137 24.4%	125 23.7%
Never	511 34.3%	8 16.0%	33 42.9%	33 42.3%	46 35.9%	178 35.4%	183 32.6%	179 34.0%
Not Applicable	240 16.1%	5 10.0%	9 11.7%	11 14.1%	32 25.0%	66 13.1%	76 13.5%	95 18.0%
Total	1491	50	77	78	128	503	562	527

QUESTION 38: **Situations in which scientists have actively objected to, resigned from or removed themselves from a project because of pressure to change scientific findings.**

		ORD Labs & Centers						
	EPA Total	NCEA	NRMRL	NERL	NHEERL	Program Offices	HQ Total	Regions Total
Frequently	29 1.9%	5 10.0%	1 1.3%	2 2.6%	1 0.8%	10 2.0%	15 2.7%	7 1.3%
Occasionally	162 10.9%	5 10.0%	8 10.5%	5 6.4%	7 5.5%	67 13.3%	75 13.3%	56 10.6%
Seldom	231 15.5%	14 28.0%	7 9.2%	7 9.0%	7 5.5%	86 17.1%	94 16.7%	96 18.3%
Never	807 54.2%	18 36.0%	51 67.1%	50 64.1%	91 71.7%	259 51.5%	287 51.1%	266 50.6%
Not Applicable	259 17.4%	8 16.0%	9 11.8%	14 17.9%	21 16.5%	81 16.1%	91 16.2%	101 19.2%
Total	1488	50	76	78	127	503	562	526

QUESTION 39: **How many activities or situations like those listed above have you personally experienced during the past 5 years?**

		Headquarters					Office of Research & Development					
	EPA Total	OAR	Water	OSWER	OPPTS	Other	HQ	NCEA	NRMRL	NERL	NHEERL	Other
0	581 39.5%	32 23.5%	24 26.7%	22 34.4%	80 39.0%	21 32.3%	7 23.3%	8 16.3%	34 45.3%	39 50.6%	78 61.4%	13 44.8%
1–5	655 44.6%	83 61.0%	45 50.0%	32 50.0%	90 43.9%	29 44.6%	16 53.3%	29 59.2%	31 41.3%	26 33.8%	41 32.3%	14 48.3%
6–10	175 11.9%	14 10.3%	17 18.9%	5 7.8%	26 12.7%	14 21.5%	4 13.3%	5 10.2%	9 12.0%	9 11.7%	5 3.9%	1 3.4%
11–20	34 2.3%	4 2.9%	2 2.2%	4 6.3%	6 2.9%	1 1.5%	2 6.7%	2 4.1%	0 0.0%	1 1.3%	2 1.6%	0 0.0%
More Than 20	25 1.7%	3 2.2%	2 2.2%	1 1.6%	3 1.5%	0 0.0%	1 3.3%	5 10.2%	1 1.3%	2 2.6%	1 0.8%	1 3.4%
Total	1470	136	90	64	205	65	30	49	75	77	127	29

	Regional Offices									
	1	2	3	4	5	6	7	8	9	10
0	12 44.4%	23 48.9%	15 41.7%	19 45.2%	50 47.2%	19 55.9%	16 50.0%	15 37.5%	21 26.6%	33 41.2%
1-5	11 40.7%	22 46.8%	13 36.1%	19 45.2%	45 42.5%	9 26.5%	11 34.4%	17 42.5%	33 41.8%	39 48.8%
6-10	4 14.8%	2 4.3%	6 16.7%	3 7.1%	10 9.4%	6 17.6%	3 9.4%	5 12.5%	19 24.1%	8 10.0%
11-20	0 0.0%	0 0.0%	2 5.6%	0 0.0%	0 0.0%	0 0.0%	1 3.1%	2 5.0%	5 6.3%	0 0.0%
More Than 20	0 0.0%	0 0.0%	0 0.0%	1 2.4%	1 0.9%	0 0.0%	1 3.1%	1 2.5%	1 1.3%	0 0.0%
Total	27	47	36	42	106	34	32	40	79	80

Note: OAR includes OAQPS and NVFEL respondents, who are not located at EPA headquarters.

Breakdown of Question 40 Responses According to Respondents' Length of Time Working at the EPA (Question 42)

Question 40: If you compare the past 5 years to the 5-year period prior to it (from 5 to 10 years ago), would you say activities or situations like those listed above are occurring:		Question 42: I have been working at the EPA for:				
	Question 40 Total	Less Than One Year	1-5 Years	6-10 Years	11-15 Years	More Than 15 Years
More Often than Before	508 34.4%	0 0.0%	16 6.9%	78 31.3%	54 40.3%	355 42.9%
About the Same as Before	330 22.4%	1 4.8%	11 4.7%	46 18.5%	28 20.9%	241 29.1%
Less Often than Before	65 4.4%	0 0.0%	6 2.6%	16 6.4%	9 6.7%	34 4.1%
Don't Know	572 38.8%	20 95.2%	200 85.8%	109 43.8%	43 32.1%	197 23.8%
Total Respondents	1464	21	233	249	134	827

Breakdown of Question 5 Responses According to Respondents' Length of Time Working at the EPA (Question 42)

Question 5: I am allowed to publish work in peer-reviewed scientific journals regardless of whether it adheres to agency policies or positions.		Question 42: I have been working at the EPA for:				
	Question 40 Total	Less Than One Year	1-5 Years	6-10 Years	11-15 Years	More Than 15 Years
Strongly Agree	132 8.4%	4 19.1%	27 11.3%	24 9.5%	7 5.1%	60 7.2%
Agree	350 22.2%	5 23.8%	58 24.4%	57 22.5%	38 27.9%	178 21.4%
No Opinion	464 29.4%	7 33.3%	74 31.1%	69 27.3%	33 24.3%	242 29.2%
Disagree	203 12.9%	1 4.8%	21 8.8%	38 15.0%	25 18.4%	109 13.1%
Strongly Disagree	88 5.6%	0 0.0%	13 5.5%	13 5.1%	6 4.4%	52 6.3%
Not Applicable	341 21.6%	4 19.1%	45 18.9%	52 20.6%	27 19.9%	189 22.8%
Total Respondents	1578	21	238	253	136	830

Breakdown of Question 21 Responses According to the Number of Incidents of Political Interference Experienced during the Past Five Years (Question 39)

Question 21: Over the past few years my personal job satisfaction at the EPA has:		Question 39: How many activities or situations like those listed above have you personally experienced during the past 5 years?				
	Question 21 Total	0	1-5	6-10	11-20	More Than 20
Increased	328 21.3%	175 30.1%	114 17.4%	19 10.9%	4 11.8%	2 8.0%
Decreased	670 43.5%	152 26.2%	317 48.5%	134 76.6%	24 70.6%	19 76.0%
Stayed the Same	501 32.6%	233 40.1%	210 32.1%	22 12.6%	6 17.6%	2 8.0%
No Opinion	40 2.6%	21 3.6%	13 2.0%	0 0.0%	0 0.0%	2 8.0%
Total Respondents	1539	581	654	175	34	25

APPENDIX C

EPA Response to UCS Survey Mailing

In response to the initial survey mailing from UCS and the Center for Survey Statistics and Methodology at Iowa State, managers at several EPA offices and locations sent emails urging their employees not to fill out the survey. Both the EPA Office of General Counsel and the Computer Security Office later reviewed the survey website, questions, and procedures, and concluded that there were no ethical, legal, or security reasons why EPA employees could not complete the survey.

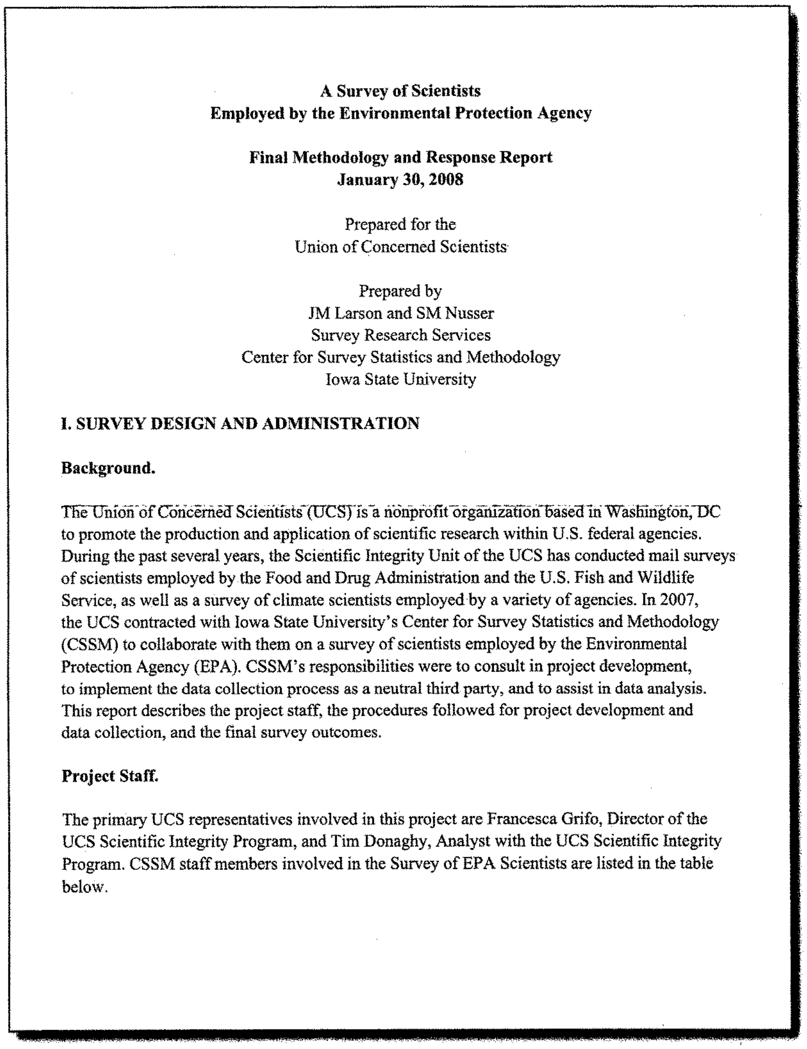
The following email message was sent from Peggy Love to the EPA's OGC National Ethics Officials on June 28, 2007, and was forwarded to numerous EPA employees:

> I have learned that there are no legal reasons to prevent EPA employees from completing the attached research study of EPA Scientists. From an ethics perspective, the survey recommends that folks complete it on their personal time and that would fall under EPA's limited use policy.
>
> This is not a government sponsored survey. The Union of Concerned Scientists is funded by large organizations which are listed in their annual report. The e-mail addresses of EPA employees were obtained from public sources including the locator and old EPA phone books which are available on Amazon.com. The results of the survey will be compiled by the Center for Survey Statistics & Methodology (CSSM) at Iowa State University and presented to the Union of Concerned Scientists. A meeting will be requested with the Administrator to share the results of the survey and the results will be posted on their website.
>
> Please advise your folks that if they received this survey and would like to complete it, they may do so.
>
> Thank you.
> Peggy Love
> Attorney (Ethics)
> Deputy Ethics Official (DEO)
> Office of General Counsel
> 7439 AR-N
> (202) 564-1784

APPENDIX D
CSSM Methodology Report

This appendix provides the Final Methodology and Response Report, completed by the Center for Survey Statistics and Methodology at Iowa State University after the close of the survey. The CSSM report offers additional detail on the survey design, implementation, data collection, and analysis. This appendix also includes the text that appeared on the first and last screens of the Web-based survey, as well as the initial email and letter sent to survey recipients.

The UCS report specifies a different total response rate than the CSSM report because UCS excluded 395 individuals whose email address returned as undeliverable.



A Survey of Scientists
Employed by the Environmental Protection Agency

Final Methodology and Response Report
January 30, 2008

Prepared for the
Union of Concerned Scientists

Prepared by
JM Larson and SM Nusser
Survey Research Services
Center for Survey Statistics and Methodology
Iowa State University

I. SURVEY DESIGN AND ADMINISTRATION

Background.

The Union of Concerned Scientists (UCS) is a nonprofit organization based in Washington, DC to promote the production and application of scientific research within U.S. federal agencies. During the past several years, the Scientific Integrity Unit of the UCS has conducted mail surveys of scientists employed by the Food and Drug Administration and the U.S. Fish and Wildlife Service, as well as a survey of climate scientists employed by a variety of agencies. In 2007, the UCS contracted with Iowa State University's Center for Survey Statistics and Methodology (CSSM) to collaborate with them on a survey of scientists employed by the Environmental Protection Agency (EPA). CSSM's responsibilities were to consult in project development, to implement the data collection process as a neutral third party, and to assist in data analysis. This report describes the project staff, the procedures followed for project development and data collection, and the final survey outcomes.

Project Staff.

The primary UCS representatives involved in this project are Francesca Grifo, Director of the UCS Scientific Integrity Program, and Tim Donaghy, Analyst with the UCS Scientific Integrity Program. CSSM staff members involved in the Survey of EPA Scientists are listed in the table below.

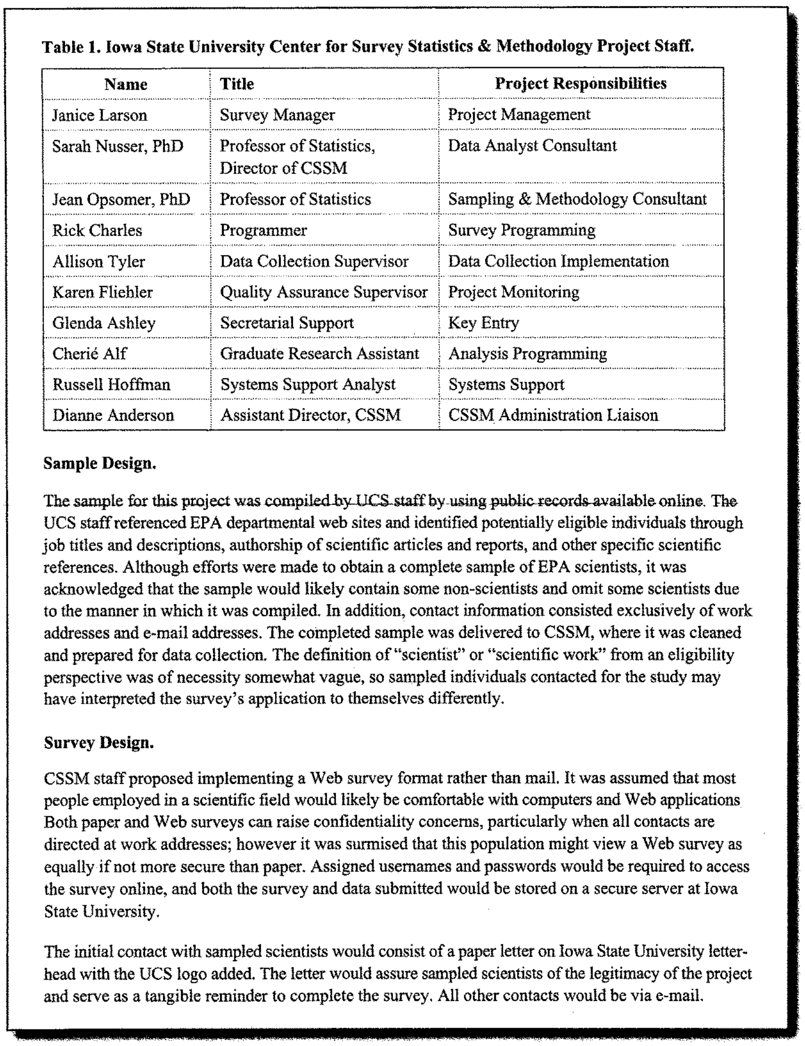


Table 1. Iowa State University Center for Survey Statistics & Methodology Project Staff.

Name	Title	Project Responsibilities
Janice Larson	Survey Manager	Project Management
Sarah Nusser, PhD	Professor of Statistics, Director of CSSM	Data Analyst Consultant
Jean Opsomer, PhD	Professor of Statistics	Sampling & Methodology Consultant
Rick Charles	Programmer	Survey Programming
Allison Tyler	Data Collection Supervisor	Data Collection Implementation
Karen Fliehler	Quality Assurance Supervisor	Project Monitoring
Glenda Ashley	Secretarial Support	Key Entry
Cherié Alf	Graduate Research Assistant	Analysis Programming
Russell Hoffman	Systems Support Analyst	Systems Support
Dianne Anderson	Assistant Director, CSSM	CSSM Administration Liaison

Sample Design.

~~The sample for this project was compiled by UCS staff by using public records available online. The~~ UCS staff referenced EPA departmental web sites and identified potentially eligible individuals through job titles and descriptions, authorship of scientific articles and reports, and other specific scientific references. Although efforts were made to obtain a complete sample of EPA scientists, it was acknowledged that the sample would likely contain some non-scientists and omit some scientists due to the manner in which it was compiled. In addition, contact information consisted exclusively of work addresses and e-mail addresses. The completed sample was delivered to CSSM, where it was cleaned and prepared for data collection. The definition of "scientist" or "scientific work" from an eligibility perspective was of necessity somewhat vague, so sampled individuals contacted for the study may have interpreted the survey's application to themselves differently.

Survey Design.

CSSM staff proposed implementing a Web survey format rather than mail. It was assumed that most people employed in a scientific field would likely be comfortable with computers and Web applications Both paper and Web surveys can raise confidentiality concerns, particularly when all contacts are directed at work addresses; however it was surmised that this population might view a Web survey as equally if not more secure than paper. Assigned usernames and passwords would be required to access the survey online, and both the survey and data submitted would be stored on a secure server at Iowa State University.

The initial contact with sampled scientists would consist of a paper letter on Iowa State University letterhead with the UCS logo added. The letter would assure sampled scientists of the legitimacy of the project and serve as a tangible reminder to complete the survey. All other contacts would be via e-mail.

II. SURVEY IMPLEMENTATION AND PROCEDURES

Survey Development and Programming.

The EPA survey was developed by UCS staff in consultation with CSSM. Many of the questions were similar to those used by the UCS in previous surveys, with revisions primarily relating to its EPA application and neutrality issues. The survey (Appendix A) consisted of approximately 40 items. CSSM staff submitted a project application with copies of the final survey document and proposed correspondence to the Iowa State University Institutional Review Board, and project approval was received on June 14, 2007.

The online survey was programmed in June of 2007 by CSSM staff. The online survey instrument pages were coded with standard HTML, with JavaScript for client-side controls and Perl CGI scripting for server side controls. The instrument was deployed to the Center's web server.

The layout of the web instrument was designed using TDM (Tailored Design Method) protocols for maximizing respondent comprehension and ease of navigation with online forms. Many of the questions were constructed in a table format, and a minimal amount of scrolling was required to view some questions.

CSS (Cascading Style Sheets) were used to control layout, font size and style, and color, thus accommodating differing window sizes and screen resolutions, and allowing users who need to override these choices for accessibility reasons to do so.

The online survey was tested and adjustments were made as needed, with a final version available on June 25, 2007.

Site Security.

Access to Internet survey sites at Iowa State University is restricted through the requirement of digital authenticated authorization. For this survey, each sampled EPA scientist was assigned a unique username and password to be entered at the survey homepage in order to gain access to the survey itself. The username served as a Case ID, and a combination of the two made survey access by unauthorized persons highly unlikely. Instructions on the survey homepage and in the advance letter and e-mails provided a name, toll-free telephone number, and e-mail address for Center project staff who would be available to assist with any difficulties encountered in accessing the survey as well as to answer questions about the survey itself.

Data Collection Procedure.

The sample of EPA scientists was provided to CSSM in three waves due to the difficulty of compiling sample information. Each wave was checked by CSSM staff and duplicate listings were removed from the samples before they were released for use. The first wave was comprised of 4838 names, the second contained 733 names, and the third contained 464, bringing the total sample size to 6035. The samples contained names, location/division, and contact information. Each sample member was sent a letter printed on CSSM letterhead with the UCS logo in the lower right corner. The letter (Appendix B) explained the purpose of the survey, the confidential and voluntary nature of the survey, and procedures for completing it. It included the survey web site and a unique user name and password to use to access the survey. Contact information was provided for both CSSM and UCS staff and recipients were encouraged to contact project staff if they had questions or felt they had been contacted in error. A few days later email invitations with the same information were sent to the same individuals. The e-mail contained a link to the survey web site. Apparently some letters reached their destination within a few days, while others were delayed and not delivered for two or more weeks. This seemed to be a function of varying protocols within different EPA units; and based on the e-mails and telephone calls received by CSSM, it resulted in some confusion or concern for some people.

Approximately 450 e-mails bounced back to CSSM as undeliverable. These were checked with the online EPA locator to verify the accuracy of the address and were resent if corrected addresses were available. Follow-up emails (Appendix C, D, and E) were sent to remind employees of the opportunity to complete the survey and also to advise them that the EPA legal and computer security departments had ruled that the survey was legal and posed no security threat to EPA computers or employees.

The three sample waves followed the same contact procedures and protocols but with varying contact dates. These are listed in the table below.

Table 2. Contact Schedule for Sample Waves.

	Wave 1 N = 4838	**Wave 2** N = 733	**Wave 3** N = 464
Letter sent (US Mail)	6/25/07	7/20/07	8/8/07
E-Mail notification	6/27/07	7/27/07	8/14/07
E-Mail reminder 1	7/11/07	8/2/07	8/20/07
E-Mail reminder 2	7/18/07	8/10/07	8/24/07
E-Mail reminder 3	7/30/07	8/14/07	8/30/07

CSSM staff received and responded to over 600 e-mails and telephone calls from individuals who requested additional information about the survey or felt that the survey did not apply to them. Respondents who were not employed as scientists or in a science-related capacity with the EPA were classified as ineligible and eliminated from future contacts.

Respondents were allowed to access their survey as often as they wished using assigned usernames and passwords. If a respondent accessed the survey multiple times, any responses from earlier visits were stored and visible upon re-entering the survey. In addition, answers to specific items could be changed as often as desired. All attempts to access the survey, both successful and unsuccessful, as well as all responses were stored in the survey database.

The data collection period closed on September 7, 2007. The resulting data file was edited and cleaned in SAS using frequencies and cross tabulations. The final data delivery consisted of an Excel data file, frequency file, open text file, and coding manual.

III. SURVEY PROCESS OUTCOMES AND RESPONSE RATE

Final results are itemized in Table 3 below. There were 221 individuals classified as ineligible, because they were not employed at the EPA in a scientific capacity. This resulted in an eligible sample of 5814. There were 395 cases in which all e-mail messages bounced as undeliverable and no locating information was available. Although it is suspected that these individuals are no longer employed by the EPA and would therefore be ineligible, CSSM staff was unable to verify that information and therefore those cases are considered part of the overall survey non-response. There were 10 individuals who were unreachable on special assignment for a period of several months, including the entire data collection period, and were classified accordingly. These are also considered part of overall survey non-response. Included among the 3750 general non-respondents are 18 individuals who started the survey but did not complete enough of it to be included in the final data set. In addition, 73 individuals actively refused to participate. Completed surveys were received from 1586 EPA employees.

When adjusted for eligibility, 1586 eligible responses were received from the adjusted eligible sample of 5814, for a response rate of 27.3%. The response rate is calculated as the ratio of completed surveys to the total eligible sample.

Table 3. Final Dispositions and Response Rate.

	#	%	#	%
Total Sample	6035	100.0%		
Ineligible	221	3.7%		
Total Eligible Sample	5814	96.3%		100.0%
Refusals			73	1.3%
Unavailable for study duration			10	0.2%
No E-mail available			395	6.8%
Non-Response			3750	64.5%
Completed Surveys			**1586**	**27.3%**
Response Rate	**27.3 %**			

IV. SURVEY ANALYSIS

Data analyses were conducted as requested by UCS. This involved defining variables for analysis, computing tabular summaries and testing for independence among variables. All analyses were run in the SAS statistical analysis system.

Derived analysis variables.

In most cases, responses from the survey could be used to summarize the data. In some cases, it was necessary to create variables from the survey responses for analysis.

In response to question 3, which asked the employee to identify what their scientific work at the EPA primarily involves, many respondents gave multiple responses. Indicator variables were created for each of the fifteen possible responses to the question so that the total number of individuals whose work involved a task could be calculated. These fifteen indicator variables were used in the analyses as the responses to question 3.

A new variable was created for the identification of the individual's organizational unit. The organizational unit was initially defined as the combination of the employee's location and division. For some of the possible combinations of location and division, the cell size was too small to be used in the analyses. In order to create adequate sample sizes, some of the organizational units were collapsed. Collapsing rules were defined by UCS and are listed in Table 4.

Table 4. Organizational Units Codes for Collapsed Cells.

Location	Division	New Organizational Unit
Ada	NRMRL	Labs Other
Las Vegas	NERL	Labs Other
Michigan	NHEERL	Labs Other
Athens	all	Labs Other
Ann Arbor	all	Labs Other
Cincinnati	NCEA	Cincinnati Other
Cincinnati	NHSRC	Cincinnati Other
Cincinnati	NERL	Cincinnati Other
RTP	NCCT	RTP Other
RTP	NCEA	RTP Other
RTP	NHSRC	RTP Other
RTP	NRMRL	RTP Other
HQ	OARM	HQ Other
HQ	NCEA	HQ ORD
HQ	NCER	HQ ORD

There is an interest in knowing the results for the divisions: NHEERL, NERL, NRMRL, and NCEA. These divisions were represented in a new variable so that the analyses could be performed on these specific divisions separately.

The variables for questions 1 (major field of training), 41 (employment grade level), and 43 (highest education level) had been recoded to incorporate some of the "Other" responses and to make cell sizes large enough for the analyses. These recoded values used in the analysis.

Frequency Tables.

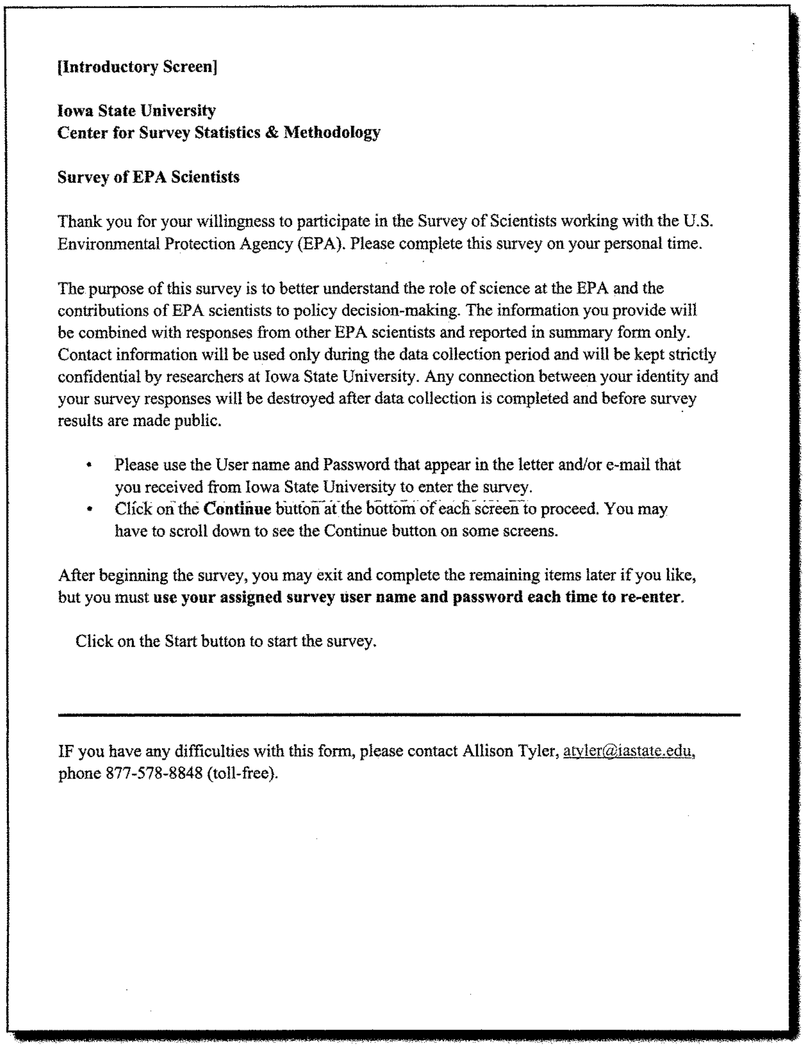
Basic frequencies were run for all variables. For each variable, summaries were generated for the frequency of respondents for each code, the percentage of respondents for each code, standard errors for the percentage, and 95% confidence intervals for the percentage.

Also of interest were cross-tabulations of all variables with the organizational unit and with questions 1 (major field of training), 2 (percentage of scientific job duties), 3 (primary scientific work), 14 (perceived resource levels), 39 (number of political situations), 41 (employment grade level), 42 (years worked at EPA), and 43 (highest education level). The indicator variables were used for question 3. Once again, the frequency, percentage, standard error for the percentage, and 95% confidence intervals for the percentage for the crossed variables were produced.

In order to be able to calculate the percentage of respondents for whom the question was deemed applicable, the not applicable responses were removed and the frequencies were reproduced for questions 5 (perception of publication freedom) and 25-38 (political interference questions).

Tests for independence.

To test for independence between the cross-tabulated responses, a chi-square test was performed for each of the variables against all other variables. In some cases the cell size is too small for the test to be considered accurate, as indicated by the SAS ouptut. UCS was advised to ignore these results.



[Introductory Screen]

Iowa State University
Center for Survey Statistics & Methodology

Survey of EPA Scientists

Thank you for your willingness to participate in the Survey of Scientists working with the U.S. Environmental Protection Agency (EPA). Please complete this survey on your personal time.

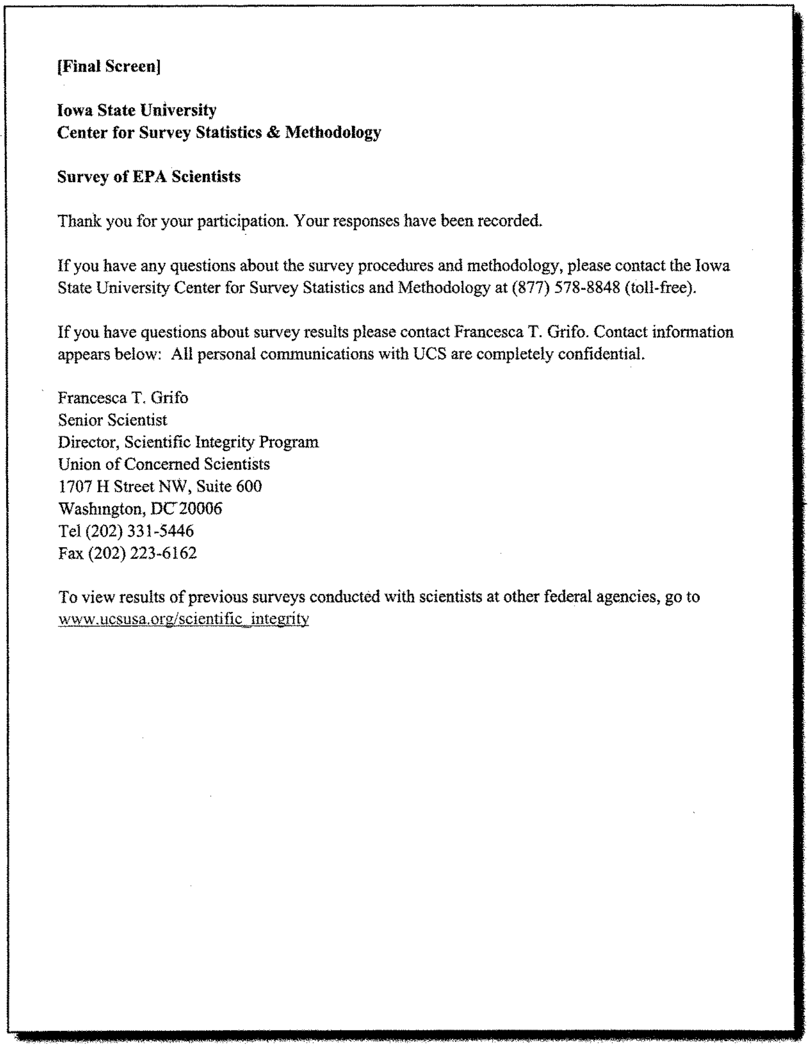
The purpose of this survey is to better understand the role of science at the EPA and the contributions of EPA scientists to policy decision-making. The information you provide will be combined with responses from other EPA scientists and reported in summary form only. Contact information will be used only during the data collection period and will be kept strictly confidential by researchers at Iowa State University. Any connection between your identity and your survey responses will be destroyed after data collection is completed and before survey results are made public.

- Please use the User name and Password that appear in the letter and/or e-mail that you received from Iowa State University to enter the survey.
- Click on the **Continue** button at the bottom of each screen to proceed. You may have to scroll down to see the Continue button on some screens.

After beginning the survey, you may exit and complete the remaining items later if you like, but you must **use your assigned survey user name and password each time to re-enter.**

Click on the Start button to start the survey.

IF you have any difficulties with this form, please contact Allison Tyler, atyler@iastate.edu, phone 877-578-8848 (toll-free).



[Final Screen]

Iowa State University
Center for Survey Statistics & Methodology

Survey of EPA Scientists

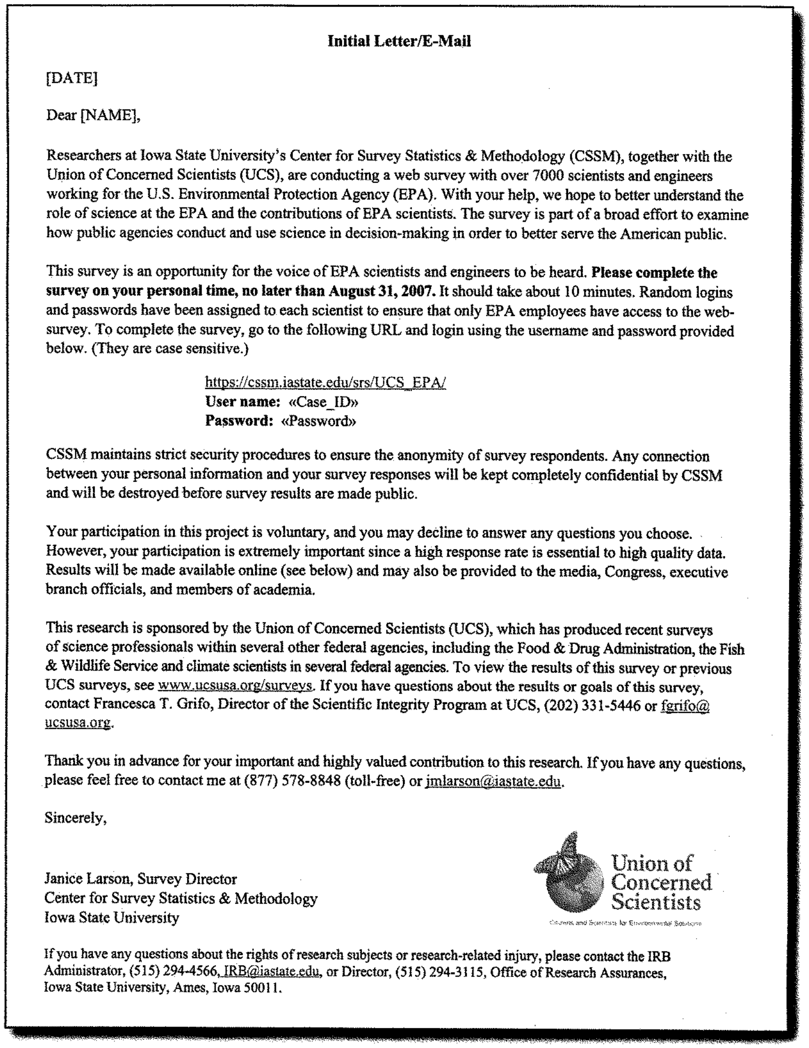
Thank you for your participation. Your responses have been recorded.

If you have any questions about the survey procedures and methodology, please contact the Iowa State University Center for Survey Statistics and Methodology at (877) 578-8848 (toll-free).

If you have questions about survey results please contact Francesca T. Grifo. Contact information appears below: All personal communications with UCS are completely confidential.

Francesca T. Grifo
Senior Scientist
Director, Scientific Integrity Program
Union of Concerned Scientists
1707 H Street NW, Suite 600
Washington, DC 20006
Tel (202) 331-5446
Fax (202) 223-6162

To view results of previous surveys conducted with scientists at other federal agencies, go to www.ucsusa.org/scientific_integrity



Initial Letter/E-Mail

[DATE]

Dear [NAME],

Researchers at Iowa State University's Center for Survey Statistics & Methodology (CSSM), together with the Union of Concerned Scientists (UCS), are conducting a web survey with over 7000 scientists and engineers working for the U.S. Environmental Protection Agency (EPA). With your help, we hope to better understand the role of science at the EPA and the contributions of EPA scientists. The survey is part of a broad effort to examine how public agencies conduct and use science in decision-making in order to better serve the American public.

This survey is an opportunity for the voice of EPA scientists and engineers to be heard. **Please complete the survey on your personal time, no later than August 31, 2007.** It should take about 10 minutes. Random logins and passwords have been assigned to each scientist to ensure that only EPA employees have access to the web-survey. To complete the survey, go to the following URL and login using the username and password provided below. (They are case sensitive.)

https://cssm.iastate.edu/srs/UCS_EPA/
User name: «Case_ID»
Password: «Password»

CSSM maintains strict security procedures to ensure the anonymity of survey respondents. Any connection between your personal information and your survey responses will be kept completely confidential by CSSM and will be destroyed before survey results are made public.

Your participation in this project is voluntary, and you may decline to answer any questions you choose. However, your participation is extremely important since a high response rate is essential to high quality data. Results will be made available online (see below) and may also be provided to the media, Congress, executive branch officials, and members of academia.

This research is sponsored by the Union of Concerned Scientists (UCS), which has produced recent surveys of science professionals within several other federal agencies, including the Food & Drug Administration, the Fish & Wildlife Service and climate scientists in several federal agencies. To view the results of this survey or previous UCS surveys, see www.ucsusa.org/surveys. If you have questions about the results or goals of this survey, contact Francesca T. Grifo, Director of the Scientific Integrity Program at UCS, (202) 331-5446 or fgrifo@ucsusa.org.

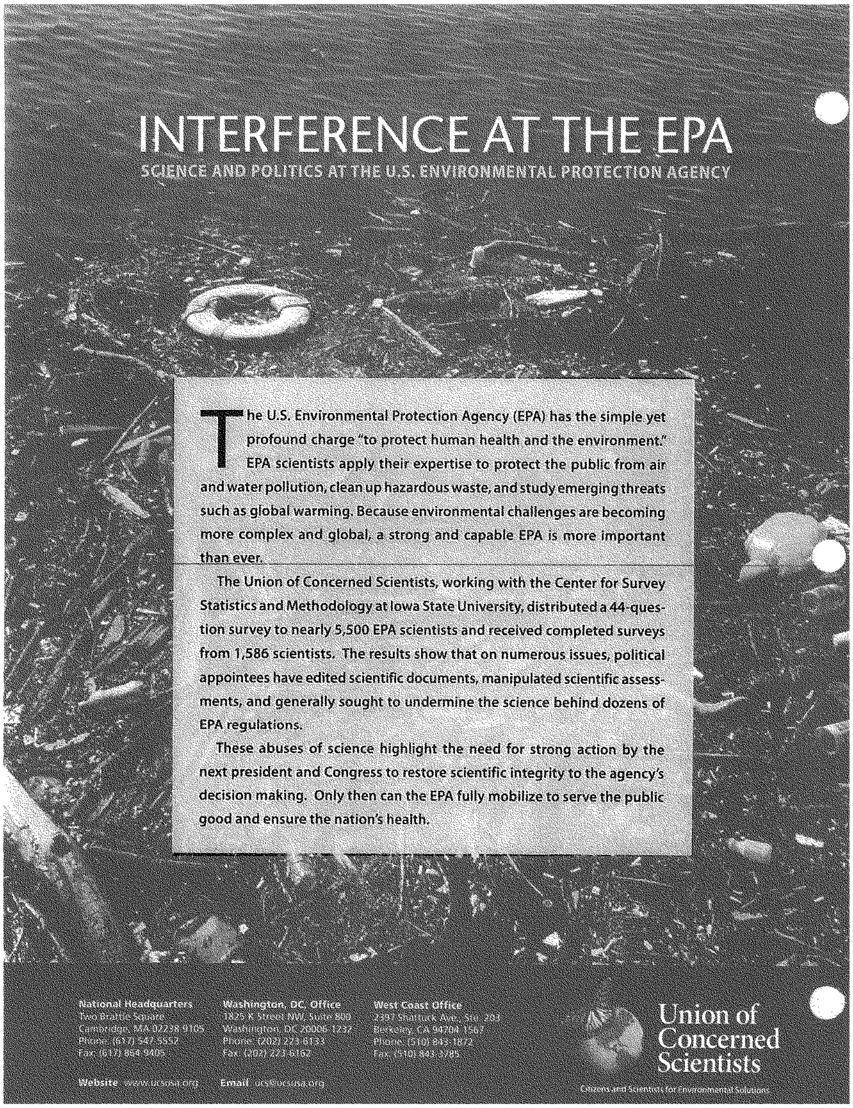
Thank you in advance for your important and highly valued contribution to this research. If you have any questions, please feel free to contact me at (877) 578-8848 (toll-free) or jmlarson@iastate.edu.

Sincerely,

Janice Larson, Survey Director
Center for Survey Statistics & Methodology
Iowa State University

Union of
Concerned
Scientists
Citizens and Scientists for Environmental Solutions

If you have any questions about the rights of research subjects or research-related injury, please contact the IRB Administrator, (515) 294-4566, IRB@iastate.edu, or Director, (515) 294-3115, Office of Research Assurances, Iowa State University, Ames, Iowa 50011.



INTERFERENCE AT THE EPA

SCIENCE AND POLITICS AT THE U.S. ENVIRONMENTAL PROTECTION AGENCY

The U.S. Environmental Protection Agency (EPA) has the simple yet profound charge "to protect human health and the environment." EPA scientists apply their expertise to protect the public from air and water pollution, clean up hazardous waste, and study emerging threats such as global warming. Because environmental challenges are becoming more complex and global, a strong and capable EPA is more important than ever.

The Union of Concerned Scientists, working with the Center for Survey Statistics and Methodology at Iowa State University, distributed a 44-question survey to nearly 5,500 EPA scientists and received completed surveys from 1,586 scientists. The results show that on numerous issues, political appointees have edited scientific documents, manipulated scientific assessments, and generally sought to undermine the science behind dozens of EPA regulations.

These abuses of science highlight the need for strong action by the next president and Congress to restore scientific integrity to the agency's decision making. Only then can the EPA fully mobilize to serve the public good and ensure the nation's health.

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Union of Concerned Scientists
Citizens and Scientists for Environmental Solutions

United States Government Accountability Office

GAO

Report to the Chairman, Committee on Environment and Public Works, U.S. Senate

March 2008

CHEMICAL ASSESSMENTS

Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System

G A O

Accountability * Integrity * Reliability

GAO
Accountability·Integrity·Reliability

Highlights

Highlights of GAO-08-440, a report to the Chairman, Committee on Environment and Public Works, U.S. Senate

March 2008

CHEMICAL ASSESSMENTS

Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA’ Integrated Risk Information System

Why GAO Did This Study

The Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) contains EPA's scientific position on the potential human health effects of exposure to more than 540 chemicals. IRIS is a critical component of EPA's capacity to support scientifically sound environmental decisions, policies, and regulations. GAO was asked to examine (1) the outcome of steps EPA has taken to ensure that IRIS contains current, credible chemical risk information, to address the backlog of ongoing assessments, and to respond to new requirements from the Office of Management and Budget (OMB); and (2) the potential effects of planned changes to the IRIS assessment process on EPA's ability to ensure that IRIS provides current, credible risk information. To do this work, GAO reviewed and analyzed EPA data and interviewed officials at relevant agencies.

What GAO Recommends

GAO recommends that EPA (1) clearly define and document an IRIS assessment process that, among other things, can be conducted within a time frame that minimizes the need for rework and (2) ensure that it can develop transparent, credible assessments by, for example, determining the types of IRIS assessments it will conduct based on EPA program needs and defining the appropriate role of other federal agencies in its IRIS assessment process. EPA agreed to consider GAO's recommendations in revising the IRIS assessment process.

To view the full product, including the scope and methodology, click on GAO-08-440. For more information, contact John B. Stephenson at (202) 512-3841 or stephensonj@gao.gov.

What GAO Found

EPA's actions since 2000 to ensure that IRIS contains current, credible risk information, to address its backlog of 70 ongoing assessments, and to respond to new OMB requirements—including increasing funding and revising the assessment process—have not enabled EPA to routinely complete credible IRIS assessments or decrease its backlog. Although in fiscal years 2006 and 2007 EPA sent 32 assessments to OMB for the first of three required external reviews, EPA finalized only 4 assessments during this period. This low level of productivity jeopardizes the viability of the IRIS database. Further, an EPA analysis indicated that many existing assessments may need to be updated, and EPA program offices and other IRIS users have requested assessments of hundreds of chemicals not yet in IRIS. Factors contributing to EPA's inability to complete IRIS assessments in a timely manner include new OMB-required reviews of IRIS assessments by OMB and other federal agencies; certain EPA management decisions, such as delaying some assessments to await new research; and the compounding effect of delays—even one delay can have a domino effect, requiring the process to essentially be repeated to incorporate changing science. As of December 2007, most of the 70 ongoing assessments had been in progress for over 5 years.

Regarding new OMB requirements, the IRIS assessment process now includes two OMB/interagency reviews of draft assessments. These reviews have resulted in involvement of other federal agencies in EPA's IRIS assessment process in a manner that limits the credibility of IRIS assessments and hinders EPA's ability to manage them. That is, the OMB/interagency reviews lack transparency—OMB considers agencies' comments on IRIS assessments to be internal executive branch documents that may not be made public. Given the importance of IRIS assessments, it is essential that input from all parties, including other federal agencies, be part of the public record. Transparency is especially important because agencies providing input include those that may be affected by the assessments should they lead to regulatory or other actions. Also, without communicating its rationale for doing so, OMB directed EPA to terminate five assessments that for the first time addressed acute, rather than chronic, exposure—even though EPA initiated this type of assessment to help it implement the Clean Air Act. Most OMB/interagency reviews completed to date have added 6 or more months to the IRIS time frames.

Such delays and credibility concerns would likely be exacerbated by further changes EPA is planning to respond to continuing concerns of other federal agencies, such as providing them with an expanded role in EPA's IRIS assessment process and discretion to suspend assessments to develop new studies for some chemicals. EPA estimates that such assessments would take up to 6 years, an estimate GAO believes is conservative in light of the assessment time frames under the current process. Suspending assessments is inefficient; alternatively, with longer-term planning, EPA could provide agencies and the public with more advance notice of assessments, enabling them to complete relevant research before IRIS assessments are started.

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Abbreviations

ATSDR	Agency for Toxic Substances and Disease Registry
DOD	Department of Defense
DOE	Department of Energy
EPA	Environmental Protection Agency
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
NASA	National Aeronautics and Space Administration
NCEA	National Center for Environmental Assessment
NCI	National Cancer Institute
NIOSH	National Institute of Occupational Safety and Health
OMB	Office of Management and Budget
ORD	Office of Research and Development
PART	Program Assessment Rating Tool
PBPK	physiologically based pharmacokinetic
RfC	inhalation reference concentration
RfD	oral reference dose
TCE	trichloroethylene

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GAO
Accountability * Integrity * Reliability
United States Government Accountability Office
Washington, DC 20548

March 7, 2008

The Honorable Barbara Boxer
Chairman
Committee on Environment and Public Works
United States Senate

Dear Madam Chairman:

The Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS)—a database integral to the agency's mission of protecting human health and the environment—contains EPA's scientific position on the potential human health effects that may result from exposure to various chemicals in the environment. IRIS data provide the fundamental scientific components needed to develop human health risk assessments. These health risk assessments, in turn, provide the foundation for risk management decisions, such as whether EPA should establish air and water quality standards to protect the public from exposure to toxic chemicals or set cleanup standards for hazardous waste sites. In addition, state and local environmental programs, as well as some international regulatory bodies, rely on IRIS health effects information in managing their environmental protection programs. Although the information in IRIS is a critical primary component of EPA's capacity to support scientifically sound decisions, policies, and regulations, many IRIS assessments are outdated, and few assessments have been completed in recent years. This has resulted in a significant backlog of incomplete chemical assessments and a growing number of outdated assessments. Further, while EPA's IRIS database currently includes about 540 chemicals, every year approximately 700 new chemicals enter commerce, any number of which could pose significant human health risks.

Overall, the goal of the IRIS assessment process is to produce quantitative estimates of cancer and noncancer effects from chronic (long term) exposure to the chemicals assessed. One impact of not having current and complete IRIS assessments of many potentially harmful chemicals is that some chemicals that pose health risks to the public may not be regulated under, for example, air or drinking water statutes, or are regulated by standards that may not sufficiently take into account the best available science on human health effects. For example, trichloroethylene (TCE), a solvent widely used as a degreasing agent in industrial and manufacturing settings, is the most frequently reported organic contaminant in groundwater and has been linked to cancer and other health hazards, according to the National Academies.[1] Yet, because of questions raised by peer reviewers about the IRIS cancer assessment for TCE, EPA withdrew the assessment from IRIS in 1989, did not initiate a new TCE assessment until 1998, and likely will not complete that assessment until 2010 or later. This delay represents an information gap of at least 21 years. Without completed IRIS assessments reflecting current risk data, EPA lacks assurance that its regulatory decisions concerning this widespread chemical reflect the best available science on its potential health effects.

While the IRIS assessment process includes numerous individual steps or activities, major assessment steps include (1) a review of the scientific literature; (2) preparation of a draft IRIS assessment; (3) internal EPA reviews of draft assessments; (4) two Office of Management and Budget (OMB)/interagency reviews, managed by OMB that provide for input from OMB as well as from other federal agencies, including those that may be affected by the IRIS assessments if they lead to regulatory or other actions; (5) an independent peer review conducted by a panel of experts; and (6) the completion of a final assessment that is posted to the IRIS Web site. EPA's assessment process has undergone a number of formal and ~~informal changes during the past several years. The agency is planning~~ further changes—particularly in the areas of external reviews and scientific data gaps—largely to address concerns of other federal agencies, such as the Department of Defense (DOD). Some of the assessment process changes have raised concerns about EPA's ability to keep its scientific assessments separate from its risk management decisions, as the National Academies recommends and EPA policy endorses.

In this context, this report examines (1) the outcome of steps EPA has taken to ensure that IRIS contains current, credible chemical risk information, to address the backlog of IRIS assessments, and to respond to new requirements from OMB; and (2) the potential effects of EPA's planned changes to the IRIS assessment process on EPA's ability to ensure that IRIS provides current, credible risk information.

In conducting our work, we obtained and analyzed information on EPA's productivity, including the number of new and completed IRIS assessments, for fiscal years 2000 through 2007; the status of IRIS assessments, as of December 1, 2007, that were in progress during fiscal year 2007; the status of IRIS assessments that have been sent to OMB for OMB/interagency review; the number of assessments in the IRIS database that may need to be updated; the resources provided to the program for fiscal years 2000 through 2007; and user needs and EPA's assessment completion goals. We interviewed EPA's National Center for Environmental Assessment officials who manage the IRIS assessment program, as well as officials from other EPA program offices and federal science and health agencies that are involved in the IRIS assessment process, to obtain their perspectives on, among other things, the current IRIS assessment process, the potential effects of the proposed changes to the process, the extent to which EPA has made progress in completing assessments and meeting user needs, and challenges EPA faces in completing assessments. In addition, we also interviewed officials from the Department of Defense, the Department of Energy (DOE), the National Aeronautics and Space Administration (NASA), and OMB to obtain their perspectives on the OMB/interagency review process and on the planned changes to the IRIS assessment process. We did not evaluate the scientific content or quality of IRIS assessments. (See app. I for a more detailed description of the methodology we employed.) We conducted our work from October 2006 to March 2008 in accordance with generally accepted government auditing standards, which require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

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[1] The National Academies comprises four organizations: the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council.

Results in Brief

EPA has taken a number of steps to help ensure that IRIS contains current, credible chemical risk information, to address its backlog of ongoing assessments, and to respond to new OMB requirements. However, to date, these changes—including increasing funding, centralizing staff conducting assessments, and revising the assessment process—have not enabled EPA to routinely complete credible IRIS assessments or decrease the backlog. That is, although EPA sent 32 draft assessments for external review in fiscal years 2006 and 2007, the agency finalized only 4 IRIS assessments during this time. Several key factors have contributed to EPA's inability to achieve a level of productivity that is needed to sustain the IRIS program and database: new OMB-required reviews of IRIS assessments by OMB and other federal agencies; the growing complexity and scope of risk assessments; certain EPA management decisions and issues, including delaying completion of some assessments to await new research or to develop enhanced analyses of uncertainty in the assessments; and the compounding effect of delays. Regarding the last factor, even a single delay in the assessment process can eventually lead to the need to repeat the assessment process to take into account changes in science and methodologies. A variety of delays have impacted the majority of the 70 assessments being conducted as of December 2007—causing them to be in process for more than 5 years. These time frames are problematic because of the substantial rework such cases often require to take into account changing science and methodologies before they can be completed. Further, because EPA staff time continues to be dedicated to completing these assessments, EPA's ability to both keep the more than 540 existing assessments up to date and initiate new assessments is limited. Importantly, EPA program offices and state and local entities have requested assessments of hundreds of chemicals not yet in IRIS, and EPA data as of 2003 indicated that the assessments of 287 chemicals in the database may be outdated—that is, new information could change the risk estimates currently in IRIS or enable EPA to develop additional risk estimates for chemicals in the database. In addition, because EPA's 2003 data are now more than 4 years old, it is likely that more assessments may be outdated now.

One of the factors that has contributed to EPA's inability to complete assessments in a timely manner—the new OMB/interagency review process—also limits the credibility of the assessments because it lacks transparency.[2] Specifically, neither the comments nor the changes EPA makes to the scientific IRIS assessments in response to the comments made by OMB and other federal agencies, including those whose workload and resource levels could be affected by the assessments, are disclosed. According to OMB, the comments it provides to EPA and EPA's disposition of them are considered internal executive branch communications that may not be made public. Further, OMB has not communicated its rationale for directing EPA to discontinue work on five IRIS assessments that EPA had sent to OMB for OMB/interagency review. These assessments, initiated to meet EPA program needs, were the first EPA IRIS assessments of short-term (acute) risks of exposure; the IRIS program historically has evaluated long-term (chronic) risks.

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[2] Transparency is relevant to both the IRIS assessment process (for example, the public availability of information about the assessment process, the input from external reviews on draft assessments, and EPA's responses to them) and the content of IRIS assessments (for example, the rationale for using specific data sets, assumptions, or models). In this report, the transparency issues we discuss primarily relate to the IRIS assessment process.

The additional assessment process changes EPA is planning would likely exacerbate delays in completing IRIS assessments and further affect their credibility. Specifically, despite the informal OMB/interagency review process that OMB required EPA to incorporate into the IRIS assessment process in 2005, certain federal agencies continue to believe they should have greater and more formal roles in EPA's development of IRIS assessments. Consequently, EPA has been working for several years to establish a formal IRIS assessment process that would expand the role of federal agencies in the process—including agencies such as DOD, which could be affected by the outcome of IRIS assessments. Some of these agencies and their contractors could face increased cleanup costs and other legal liabilities if EPA issued an IRIS assessment for a chemical that resulted in a decision to regulate the chemical to protect the public. Under EPA's planned changes, these potentially affected agencies would be able, at several points in the assessment process, to subject particular chemicals of interest to additional process steps. EPA estimates that these assessments would take up to 6 years to complete because, for example, at the discretion of these agencies, EPA would suspend the assessment process for up to 18 months so the agencies could conduct additional research to fill data gaps, rather than proceeding with currently available data. While it is important to ensure that assessments consider the best science, EPA has acknowledged that waiting for new data can result in substantial harm to human health, safety, and the environment. Further, although coordination with other federal agencies about IRIS assessments could enhance the quality of the assessments, increasing the role of agencies that may be affected by IRIS assessments in the process itself reduces the credibility of the assessments if that expanded role is not transparent. In this regard, while EPA planned to include federal agencies' comments in the public record, the process changes have been delayed since early 2007 in part because of OMB's view that agencies' comments about IRIS assessments represent internal executive branch communications that may not be made public—a view that is inconsistent with the principle of sound science that relies on, among other things, transparency.

We are making recommendations to the EPA Administrator to require the Office of Research and Development to re-evaluate its draft proposed changes to the IRIS assessment process in light of the issues raised in this report and ensure that any revised process, among other things, clearly defines and documents an IRIS assessment process that will enable the agency to develop the timely chemical risk information it needs to effectively conduct its mission. In addition, we are recommending that the EPA Administrator take steps to better ensure that EPA has the ability to develop transparent, credible IRIS assessments, including determining the types of assessments it needs to support its programs; defining the appropriate role of external federal agencies in EPA's IRIS assessment process; and managing an interagency review process in a manner that enhances the quality, transparency, timeliness, and credibility of IRIS assessments.

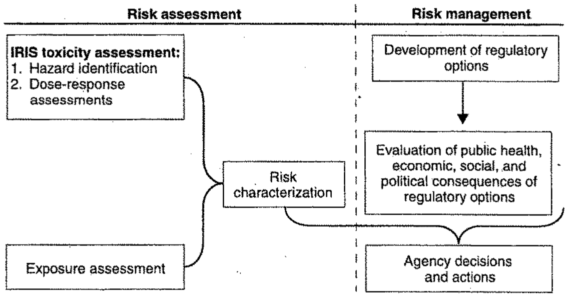
We provided EPA and OMB with a draft of this report for review and comment. EPA agreed to consider our recommendations in revising the IRIS assessment process. However, EPA stated that it believed the productivity and transparency issues discussed in the draft report were misrepresented in the title and body of the report. We disagree and believe we have fairly represented IRIS productivity and transparency issues related to the IRIS assessment process. We did, however, clarify that the transparency issues highlighted in our report focus on the IRIS assessment process rather than on the content of IRIS assessments, and we revised the report title. In its comments, OMB did not specifically address the recommendations we made to EPA but disagreed with some aspects of the report, such as our characterization of the purpose and effect of the OMB-managed interagency reviews of IRIS assessments and our conclusion that ~~interagency comments should be transparent. We disagree with OMB~~ and believe that we have fairly represented the OMB/interagency review process as well as the importance of making input from all parties publicly available to alleviate concerns of potential bias. EPA's and OMB's letters and our detailed responses are discussed further at the end of this report and in appendixes IV and V.

Background

EPA's Integrated Risk Information System (IRIS) is an important source of information on health effects that may result from exposure to chemicals in the environment. IRIS was created in 1985 to help EPA develop consensus opinions within the agency about the health effects from chronic exposure to chemicals, and its importance has increased over time as EPA program offices and the states have increasingly relied on IRIS information in making environmental protection decisions. Today, the IRIS database—which currently contains assessments of more than 540 chemicals—is heavily relied upon by EPA, state and local environmental programs, international regulatory bodies, academia, industry, and others to support risk-based decision making to protect public health and the environment. According to EPA, national and international users access the IRIS database approximately 9 million times a year. EPA's Assistant Administrator for the Office of Research and Development has described IRIS as the premier national and international source for qualitative and quantitative chemical risk information; other federal agencies have noted that IRIS data is widely accepted by all levels of government across the country for application of public health policy, providing benefits such as uniform, standardized methods for toxicology testing and risk assessment, as well as uniform toxicity values. Similarly, a private-sector risk assessment expert has stated that the IRIS database has become the most important source of regulatory toxicity values for use across EPA's programs and is also widely used across state programs and internationally.

As shown in figure 1, the toxicity assessments in the IRIS database fulfill the first two critical steps of the risk assessment process—providing hazard identification and dose-response assessment. IRIS information can then be used with the results of exposure assessments (typically conducted by EPA's program or regional offices) to provide an overall characterization of the public health risks for a given chemical in a given situation. The risk characterization information can be used to make risk management decisions designed to protect public health. The development of risk assessments is thus directly dependent on the development of toxicity assessments such as those developed in the IRIS program.

Figure 1: National Academies' Risk Assessment and Risk Management Model Used by EPA


Risk assessment
Risk management
IRIS toxicity assessment:
1. Hazard identification
2. Dose-response assessments
Development of regulatory options
Evaluation of public health, economic, social, and political consequences of regulatory options
Risk characterization
Exposure assessment
Agency decisions and actions

Source: National Academies.

Risk management, as opposed to risk assessment, involves integrating the risk characterization information generated from the risk assessment with other information, such as economic information on the costs and benefits of mitigating the risk, technological information on the feasibility of managing the risk, and the concerns of various stakeholders, to decide how to protect public health. An initial risk management decision would be to determine whether the health risks identified in a chemical risk assessment warrant regulatory or other actions. Examples of subsequent risk management decisions that could stem from a determination that action is necessary to protect public health include deciding (1) how much of a chemical a company may discharge into a river; (2) which substances may be stored at a hazardous waste disposal facility; (3) the extent to which a hazardous waste site must be cleaned up; (4) permit conditions for treatment, storage, or disposal of hazardous waste; (5) levels for air emissions; and (6) allowable levels of contamination in drinking water. Thus, as EPA has recognized, although IRIS assessments are not regulatory in nature, the quantitative IRIS values may influence many environmental decisions and may serve as a basis for regulatory consideration.

A typical IRIS assessment contains a qualitative hazard identification description and quantitative dose-response assessments. Among other things, a hazard identification description identifies the potential noncancer and cancer health effects of exposure to a chemical that research studies have suggested or determined. For example, for cancer effects, EPA describes the potential health risk using one of five weight-of-the-scientific-evidence descriptors, ranging from "carcinogenic to humans" to "not likely to be carcinogenic to humans." The quantitative assessments also address noncancer and cancer health effects and are developed if there are sufficient credible research data, primarily from either animal (toxicity) or human (epidemiology) studies to support this type of analysis. The noncancer dose-response assessments may include

- an oral reference dose (RfD)—an estimate of the daily exposure to a chemical that is likely to be without an appreciable risk of deleterious effects during a person's lifetime—expressed in terms of milligrams per kilogram, and
- an inhalation reference concentration (RfC)—an estimate of the daily exposure to a chemical that is likely to be without an appreciable risk of deleterious effects during a person's lifetime—expressed in terms of milligrams per cubic meter.

The quantitative cancer toxicity assessments include estimates of a chemical's carcinogenic potency—a "cancer slope factor" and "unit risks." Both the cancer slope factor and unit risks are estimates of the increased cancer risk (e.g., 1 in 100 people getting cancer, 1 in 1,000, 1 in 1 million, etc.) from a lifetime of exposure to a given chemical. However, the unit risk is an estimate of the increased risk for lifetime exposure at a standard concentration of a chemical in air or water (1 microgram per cubic meter of air or 1 microgram per liter in water), whereas the cancer slope factor is an estimate of the increased risk per unit dose (calculated using a dose-response curve, or a graph that shows the relationship between a dose and the proportion of exposed persons or animals that have a biologically significant response).[3]

Historically and currently, the focus of IRIS toxicity assessments has been on the potential health effects of long-term (chronic) exposure to chemicals. According to OMB,[4] EPA is the only federal agency that develops qualitative and quantitative assessments of both cancer and noncancer risks of exposure to chemicals, and EPA does so largely under the IRIS program. Other federal agencies develop qualitative cancer assessments or quantitative estimates of noncancer effects of exposure to chemicals in the environment. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) develops quantitative estimates of the noncancer effects of exposures to chemicals in the environment for exposures of up to 14 days (acute); more than 14 days but less than a year (subchronic); and 365 days and longer (chronic). While ATSDR's toxicological profiles include information from other agencies' cancer assessments, including EPA's quantitative IRIS cancer assessments, ATSDR does not develop quantitative cancer assessments. ATSDR toxicological profiles also include qualitative cancer assessments developed by the Department of Health and Human Services' National Toxicology Program and the World Health Organization's International Agency for Research on Cancer (IARC). While these latter assessments provide information on the effects of long-term exposures to chemicals, they only provide qualitative assessments of cancer risks (e.g. known human carcinogen, likely human carcinogen, etc.) and not quantitative estimates of cancer potency, which are required to conduct quantitative risk assessments.

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[3] The cancer slope factor and unit risk typically are both upper bound estimates (the plausible statistical upper limits of the true value of a quantity).

[4] OMB, Fiscal Year 2006 Program Assessment Rating Tool (PART) assessment of EPA's Human Health Risk Assessment Program.

As the IRIS database became more widely used and accepted, EPA took steps, beginning in the early 1990s, to improve and maintain the IRIS program and database. For example, the agency created an IRIS Quality Action Team that produced a report in 1994 outlining a number of recommendations for improvement, and EPA implemented a pilot program from 1995-1997 to test new operational procedures for the IRIS program. Changes under the pilot program included developing a standard toxicological review document to support each IRIS summary, incorporating peer review into the assessment process, and establishing a standing group of 18 senior health scientists to conduct the internal agency review of all IRIS draft assessments. The standing group, now called the IRIS Agency Review Committee, includes representatives from the program offices and regions. EPA also formed an IRIS implementation strategy team that developed recommendations in 1997 to improve the IRIS program and database. Key recommendations addressed the need to (1) update IRIS information, (2) establish an annual agenda for the program, (3) form a central IRIS staff to be responsible for the database and to coordinate with the program and regional offices leading individual IRIS assessments, (4) provide Internet access to the IRIS database, and (5) conduct more outreach to users.

In response, EPA formed a small centralized IRIS staff in the Office of Research and Development, National Center for Environmental Assessment (NCEA), which has implemented many of these recommendations. For example, EPA placed the IRIS database on its Web page, set up a hot line service to improve outreach with users, and started developing an annual IRIS agenda that identifies the chemicals to be assessed during the fiscal year (new and ongoing assessments) and providing this agenda to the public in a notice in the *Federal Register*. EPA also responded to the recommendations by posting external peer review drafts of IRIS assessments on EPA's Web page and considering public comments received on these drafts. As discussed below, EPA has continued to evaluate its IRIS assessment process and make changes in an effort to improve it.

EPA's Efforts to Improve the IRIS Assessment Program Have Not Produced the Desired Results

In response to criticisms and in an effort to meet the needs of the programs and entities that rely on IRIS information, EPA has continued to make a number of IRIS assessment process changes aimed at improving the timeliness, quality, consistency, and transparency of IRIS assessments. However, even with process changes and increased program funding and staffing, EPA has not been able to routinely complete credible assessments or decrease its backlog of ongoing assessments. Several key factors have contributed to EPA's inability to achieve a level of productivity that is needed to sustain the IRIS program and database, including the OMB/interagency review process managed by OMB, certain management decisions and issues regarding the IRIS program, and the compounding effect of delays. In addition, because the OMB/interagency review process is not transparent, this change also limits the credibility of IRIS assessments.

EPA Efforts to Improve IRIS Continue

Despite the many steps that EPA took throughout the 1990s aimed at improving the IRIS assessment process, the agency has continued to face criticism that the risk information in the database is outdated and of varying quality. For example, according to congressional testimony in 2000 by a risk assessment expert and a representative of a chemical industry association, the outdated and inconsistent information in IRIS represented a serious limitation that undermined the accuracy of risk assessments and risk management decisions. In addition, external parties—notably entities that may be affected by the IRIS assessments, including other federal agencies and industry—have criticized the IRIS assessment process as lacking transparency and have sought earlier input into EPA's assessment process. Further, as a result of continuing concerns that EPA and state regulators were relying on scientific information that was potentially outdated, in 2000, a Senate appropriations committee report directed EPA to conduct an assessment to determine the need to both update and add new assessments to IRIS.

In response to the criticisms and in an effort to meet the needs of the programs and entities that rely on IRIS information, EPA has continued to make a number of IRIS assessment process changes aimed at improving the timeliness, quality, consistency, and transparency of IRIS assessments. For example, EPA further centralized the assessment process, hiring additional scientists in the Office of Research and Development to lead individual IRIS assessments; in the past, chemical managers in various program offices and regions had led the assessments on a voluntary basis. EPA made this change to improve the timeliness of assessments and to address concerns about the inconsistency of assessments that the different offices were producing. In addition, EPA changed its peer review requirements, opting for peer review panels, whose meetings the agency has opened to the public, rather than obtaining written peer review comments from several experts. According to EPA, these steps were taken to provide the best possible scientific review of each assessment and to make the review process more transparent.

EPA also decided to conduct its internal agency review of assessment drafts earlier in the process. That is, the 18-member IRIS Agency Review Committee comprising EPA senior health scientists now comments on draft assessments before they are released for external review, as well as after external review comments are incorporated in the assessments. In the past, the review by the IRIS Agency Review Committee had taken place once, following the external reviews. According to EPA, this change was made to enhance peer reviews by identifying key science issues and providing external reviewers with drafts that had already been thoroughly vetted within EPA. Prior to this change, IRIS assessments had been internally peer reviewed by three or four scientists with relevant expertise in the Office of Research and Development, program offices, or regions before the assessments were sent to external peer review.[5] EPA has also added formal briefings of draft assessments to the Assistant Administrator, Office of Research and Development, at various stages in the assessment process. In addition, EPA informally elevated final IRIS assessment approval authority to the Assistant Administrator, Office of Research and Development. EPA has also delayed or suspended some assessments to await new or scientific studies.

Another key change that EPA has incorporated into the IRIS assessment process at OMB's request is an OMB/interagency review process that is managed by OMB. The purpose of these reviews is to obtain input from OMB and other federal agencies that OMB has determined have an interest in particular IRIS assessments as they are being developed in order to help ensure and increase their quality. The reviews occur at two points in the IRIS assessment process—first, after the internal agency review but before the external peer review; and second, after EPA has incorporated input from the external peer review. According to EPA officials, this OMB/interagency review process has evolved from an ad hoc review of selected IRIS assessments of interest to OMB and other federal agencies to a process that now requires, for all assessments, OMB's determination that

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[5] This internal peer review continues to be conducted during the assessment drafting stage.

EPA has satisfactorily addressed all OMB/interagency comments. This determination must be made both before EPA can provide draft assessments to external peer reviews and before EPA can finalize and post assessments on the IRIS database.

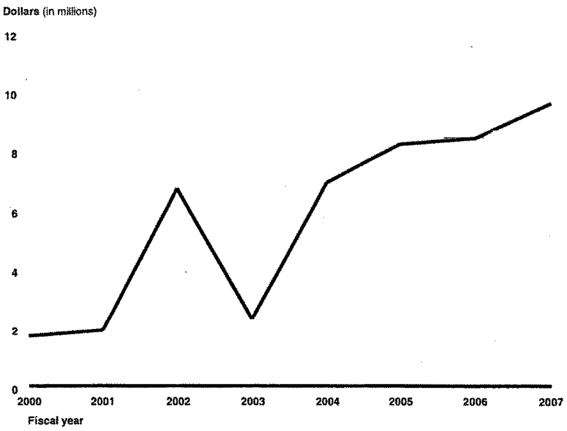
Although the IRIS assessment process continues to evolve, it currently typically includes the following steps (see app. II for a flow chart of the process):

- solicitation of chemical nominations from EPA program and regional offices, federal agencies, and the public.
- selection of chemicals to be assessed during the fiscal year (referred to as the annual agenda).
- publication of a *Federal Register* notice announcing EPA's annual agenda—the specific chemical assessments the agency intends to conduct—and requesting scientific information about these chemicals, thereby giving the public and other federal agencies an opportunity to identify relevant studies.
- a review of the scientific literature.
- development of draft IRIS toxicological reviews and summaries containing qualitative and, if sufficient information is available, quantitative risk estimates, that have undergone internal peer consultation—a peer review by three or four EPA scientists with relevant expertise.
- initial internal agency review, which includes review and comment from the 18-member EPA IRIS Agency Review Committee.
- OMB/interagency review by other federal agencies, such as DOD, DOE, and NASA, coordinated by the Office of Management and Budget; OMB informs EPA when EPA has adequately addressed interagency comments.
- external peer review by a group of independent experts, convened by an EPA contractor, the Science Advisory Board, or the National Academies, and public comment.
- a second internal agency review.
- a second OMB/interagency review; OMB informs EPA when EPA has adequately addressed interagency comments.

- EPA management review and approval.
- posting of IRIS assessments on the IRIS database, available on EPA's Web site.

In addition to EPA continuing to revise its IRIS assessment process, since fiscal year 2000, funding for the IRIS program has increased—from $1.7 million to $9.6 million in fiscal year 2007 (see fig. 2). The need for increased resources to accomplish significant IRIS improvements had been noted in the February 1997 IRIS Implementation Strategy Team Report.

Figure 2: Funding for the IRIS Program, Fiscal Years 2000-2007



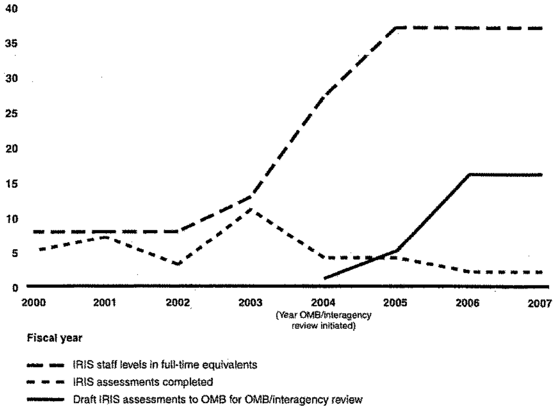
Source: GAO analysis of EPA data.

Note: In fiscal year 2002, a congressional appropriations conference committee designated $5 million to accelerate the development of new IRIS values and to update current IRIS values. According to EPA officials, this funding was provided to various EPA program offices to support the IRIS assessments that program offices were leading at that time. In addition, EPA has reprogrammed funds from some of its other programs to expand the IRIS program to support the development of IRIS assessments, especially high-priority chemicals.

Process Changes and Increased Resources Have Not Enabled EPA to Routinely Complete IRIS Assessments and Meet Users' Needs

As shown in figure 3, EPA has continued to take steps to improve the IRIS assessment process and increased program funding and staffing, but the agency has not made progress in completing IRIS assessments and reducing its backlog of ongoing assessments. Although the number of program staff has quadrupled from 8 to 37 between 2000 and 2007, EPA has, on average, completed about five IRIS assessments per year—and in fiscal years 2006 and 2007, completed only two each year. However, EPA sent 16 draft assessments to OMB for OMB/interagency review in both fiscal years 2006 and 2007 and plans to provide 16 draft assessments to OMB annually in fiscal years 2008 through 2012. Further, in its fiscal year 2008 budget justification documents, EPA said it plans to complete 8 IRIS assessments in fiscal year 2008, noting that completion of assessments, rather than providing drafts to OMB, is the most important outcome.

Figure 3: Number of Completed IRIS Assessments, Draft Assessments to OMB, and IRIS Staff in Full-Time Equivalents, Fiscal Years 2000-2007



Source: GAO analysis of EPA data.

During fiscal year 2007, EPA had 77 ongoing IRIS assessments. As of December 1, 2007, 70 of these were still in progress—2 were completed in fiscal year 2007 and 5 were discontinued at the direction of OMB.[6] Representing EPA's first efforts to develop IRIS assessments covering acute (short-term) exposure to chemicals, EPA initiated them in 2004 to meet EPA program needs, including, for example, to help it implement the Clean Air Act. In November 2007, EPA officials told the members of the Board of Scientific Counselors committee evaluating EPA's health risk assessment program that OMB did not explain to EPA why it was directing the agency to terminate these IRIS assessments.

Of the 70 assessments still in progress as of December 1, 2007, 48 have been in progress for more than 5 years, and 12 of those for more than 9 years. As figure 4 shows, many of these assessments are either being drafted or are undergoing internal agency review. Additionally, 19 assessments are undergoing one of the two OMB/interagency reviews managed by OMB, and 5 of the assessments have been suspended by EPA for various reasons, including waiting for new research studies that have yet to be completed.

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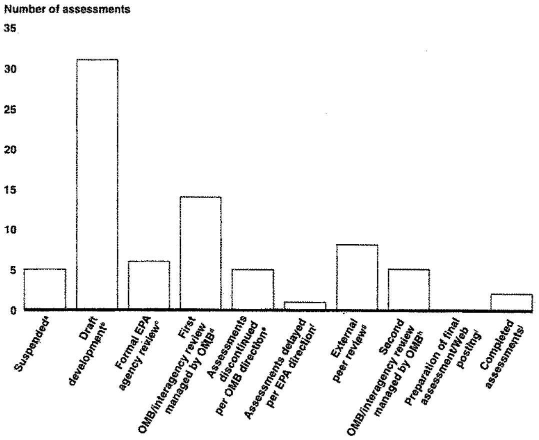
[6] OMB did not include these five assessments towards EPA's fiscal year 2006 annual performance goals and thus does not acknowledge that EPA sent 16 draft assessments to it for OMB/interagency review that fiscal year.

Figure 4: December 2007 Status of IRIS Assessments That EPA Reported as Ongoing in Fiscal Year 2007



Source: GAO analysis of EPA information.

[a] EPA has suspended five IRIS assessments for several reasons, including waiting for additional research, reevaluating the need for an assessment, and potentially broadening the scope of an assessment.

[b] This phase includes conducting literature searches, drafting assessments, and incorporating comments from an internal peer review process; it is concluded when the IRIS Program Director provides the draft and support documents for review by EPA's IRIS Agency Review Committee.

[c] This phase includes the review by EPA's IRIS Agency Review Committee and revisions in response to the review; it is concluded when the NCEA Associate Director for Health transmits a draft to OMB.

[d] This phase encompasses the first OMB/interagency review managed by OMB; revisions in response to the review; negotiations among EPA, OMB, and other federal agencies over changes to the draft and the content of the charge questions for the external peer reviewers; and briefing of the Assistant Administrator for the Office of Research and Development (ORD). It is concluded when OMB informs EPA that issues have been resolved and the assessment can proceed to the next step—external peer review.

[e] In November 2007, EPA said that in 2006 OMB requested and then in 2007 directed EPA to discontinue the five IRIS assessments covering acute exposures that EPA had sent to OMB for OMB/interagency review from July to September 2006.

[f] One assessment has been delayed by EPA for almost 2 years pending the development of an acceptable uncertainty analysis.

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[g] This phase encompasses public review and comment, the external peer review conducted by an independent panel, and incorporation of draft revisions in response to peer review and public comments. It is concluded when the NCEA Associate Director for Health transmits a revised draft to OMB for the second OMB/interagency review it manages.

[h] This phase encompasses the second review by EPA's IRIS Agency Review Committee; the second OMB/interagency review managed by OMB; revisions in response to comments received from agency and OMB/interagency review; negotiations among EPA, OMB, and the other federal agencies over changes; and briefing of the Assistant Administrator for ORD. It is concluded when ORD, the IRIS Agency Review Committee, and other federal agencies resolve all issues, OMB informs EPA that issues have been resolved, and a revised IRIS assessment is sent for preparation of a final IRIS assessment.

[i] This phase encompasses the final preparation of the IRIS summary and toxicological review and the review and clearance by the NCEA Director. It is concluded when the assessment is posted on the IRIS Web site after the Assistant Administrator, ORD, approves a fact sheet about the assessment prepared by the chemical manager.

[j] EPA completed two assessments in July and September 2007.

In addition to the current backlog of 70 ongoing and suspended IRIS assessments, EPA data from 2001 through 2003 indicated that 287 of the chemicals in the IRIS database may potentially need to be updated. Specifically, EPA reviewed the scientific literature on the 460 chemicals in the database not being reassessed to identify assessments that may need to be updated in light of new studies or information that could potentially ~~change the risk estimates currently~~ in ~~the IRIS assessments. In addition,~~ while conducting these literature reviews, EPA identified new studies or information that would enable the agency to develop additional risk estimates (e.g., add an estimate, such as an RfD or cancer potency estimate, for assessments lacking such estimates). EPA's "screening level review" found new information that could potentially (1) change an existing risk estimate for 169 chemicals and/or (2) allow EPA to develop additional risk estimates for 210 chemicals. Although EPA identified these chemicals as candidates for reassessment, as of fiscal year 2007, the agency had initiated reassessments of only a few of these chemicals. Further, because the screening levels were completed more than 4 years ago, it is likely that more assessments may now be outdated.

EPA officials said they have initiated another screening level review that they expect to be completed by July 2008. Importantly, in its performance assessment of EPA's human health risk assessment program, which includes IRIS, OMB considers health assessment values in IRIS as out of date if they were developed more than 10 years ago and where new scientific information has been identified that could change the health assessment value. This designation highlights the need for EPA to become productive in completing its IRIS assessments if it is to remain a viable and credible assessment resource. We note that EPA recently formed a new working group that will specifically address chemical assessments that are over 10 years old and for which new information is available. This group's efforts are currently in the planning stages, and an EPA official involved in this group indicated that the agency expects to begin work on this effort by March 2008.

Although EPA has stated its intent that the IRIS database be updated and expanded to include new assessments requested by IRIS users as soon as "practically possible," the current backlog continues to present a practical impediment to doing so. Because of the backlog, for example, EPA did not initiate new assessments in fiscal years 2006 and 2007.[7] In fact, key IRIS users—two EPA program offices—specifically requested that the IRIS program management focus its resources on expediting the completion of ongoing IRIS assessments important to their regulatory and cleanup responsibilities rather than initiating new assessments in fiscal year 2007. For example, the Office of Solid Waste and Emergency Response identified 29 assessments that were important to that office and asked EPA to finish these IRIS assessments before initiating others. In addition, the Office of Air identified 28 high-priority IRIS assessments that it needed to fulfill its regulatory mandates,[8] 14 of which it identified as being of the "highest priority" and the other as "high priority;" IRIS reviews for 12 of the chemicals of highest priority are in progress, but most of these assessments are still either being drafted or are undergoing an internal agency review. In terms of new assessments that will be needed for EPA's air toxics program, an official in the Office of Air and Radiation said there were about 12 to 20 air toxics of concern nationwide for which IRIS risk information is needed and about 50 or so uncommon air toxics emitted in isolated "hot spots" (e.g., near a chemical plant in sparsely populated areas) where a small number of people who live nearby—perhaps 200 or so—are exposed to relatively high doses of these air toxics. He said it is more difficult to get approval for assessments of such chemicals because of the small number of people potentially affected, even though these chemicals may be very harmful to human health and the environment.

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[7] EPA has, in some cases, divided an ongoing assessment into two assessments. For example, in fiscal year 2007, the arsenic assessment covering both cancer and noncancer risks, which was started in 2003, was divided into two separate assessments. Although the noncancer assessment was started in 2003, IRIS Track, which tracks the status of ongoing assessments, shows a 2007 start date for the IRIS noncancer assessment.

[8] The two offices identified the same priority chemicals in eight cases.

Moreover, as discussed above, EPA program offices and state and local entities have identified needs for assessments of hundreds of chemicals not yet in IRIS. For example, in its 2003 needs assessment report, EPA reported that about half of the chemicals and chemical classes that IRIS users had nominated for assessment were not included in IRIS.[9] Reasons that IRIS users nominated these chemicals included to support anticipated rule making, to support agency or state implementation priorities, to address children's health concerns, and to address the widespread occurrence of a chemical at contaminated sites and in groundwater. Unmet IRIS needs affect IRIS data users both within and outside EPA. For example, EPA's Office of Research and Development noted in its 2003 *Air Toxics Multi-Year Plan* that quantitative assessment values (for noncancer and cancer health effects) for many high-priority air toxics that are needed to support site-specific efforts and regulatory decisions are "missing." Along these same lines, in its *Office of Solid Waste Integrated Research and Development Plan for the Hazardous Waste Identification Rule*, EPA's Office of Research and Development identified 460 chemicals of potential concern and reported that roughly 200 of these lack quantitative assessment values (estimates of the risk of cancer and noncancer effects of the chemicals). Non-EPA users also are affected by the lack of IRIS values. According to the preliminary results of an EPA project aimed at determining how IRIS is used by non-EPA decision makers,[10] non-EPA users have one primary criticism regarding IRIS—they are frustrated by the lack of new assessments, particularly for "controversial" chemicals. These users reported that the absence of an IRIS assessment creates enormous challenges for state regulatory agencies and significant uncertainty for regulatory parties.

Although EPA's 2003 needs assessment report had identified a potential need to complete 50 IRIS assessments annually to meet user needs, the agency has not finalized more than 11 assessments a year during the past 10 years. As figure 3 shows, productivity has, in fact, declined since 2003, with EPA completing 4 assessments in fiscal year 2005 and 2 each in fiscal years 2006 and 2007. EPA's updated multiyear plan estimates incremental increases in the number of IRIS assessments EPA will complete in fiscal years 2008 through 2011, at which point EPA's annual goal is to complete

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[9] The other nominations were for chemicals in IRIS with outdated assessments.

[10] The preliminary findings of the Use of IRIS Project were presented during the EPA's Board of Scientific Counselors' Human Health Risk Assessment Subcommittee meeting on November 15, 2007.

16 IRIS assessments.[11] We note that even if EPA were to overcome the significant productivity difficulties it has experienced in recent years and meet this goal of completing 16 assessments a year beginning in 2011, it is not clear that this level of productivity would meet the needs of EPA program offices and other users, given the current status of the database. For example, in November 2007, the Deputy Administrator of EPA's Region 2 told the Board of Scientific Counselors panel reviewing EPA's human health risk assessment program that even 16 IRIS assessments per year would not meet their chemical assessment needs. Although funding for the IRIS program has increased since 2000, we note that fiscal year 2007 funding of $9.6 million represents approximately 0.1 percent of EPA's $7.3 billion annual budget.

It is a positive step that EPA delivered 32 IRIS assessments to OMB for OMB/interagency review in fiscal years 2006 and 2007. However, in general, the IRIS assessments sent to OMB during this period were on less controversial chemicals. In its December 2005 multiyear plan, EPA specified 10 major assessments that would be sent for external review in fiscal years 2006 and 2007. As of December 1, 2007, only 2 of these assessments had been sent for OMB/interagency review.[12] In order to meet user needs and therefore enable EPA to more effectively protect public health, it will be important for EPA to make progress on the assessments of the more controversial chemicals, which tend to be those to which people are more widely exposed.

Lastly, while EPA's assessment process changes have resulted in EPA providing the public with more information about IRIS assessments, some of the information provided in *Federal Register* notices and in the IRIS database itself is not accurate or is incomplete. For example, some assessments that have been suspended have continued to be identified as ongoing, and information on the status of the individual assessments provided in a system called IRIS Track has not been kept up to date. Regarding this latter point, we found that more EPA chemical managers started updating this database as a result of our review. Nonetheless, some of the milestone estimates remained outdated, and the milestones in IRIS Track did not reflect the current assessment process. We note that in November 2007, EPA created a new IRIS Web page, updating and consolidating some of the milestones to better reflect the current process. However, two key milestones—the second OMB/interagency and EPA internal agency reviews—are still not identified.

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[11] EPA, *Human Health Risk Assessment Multi-Year Plan* (Washington, D.C., 2007).

[12] In its 2005 multiyear plan EPA, specified that it would send the assessments for acrylamide, MTBE, naphthalene, tetrachloroethylene (perc), acrylonitrile, formaldehyde, methanol, methylene chloride, trichloroethylene, and dioxin for external review during fiscal years 2006 and 2007. Only acrylamide and tetrachloroethylene (perc) have been sent to OMB for OMB/interagency review.

EPA's Productivity Problems Stem from Several Key Factors

In our view, several key factors have contributed to EPA's inability to achieve a level of productivity that is needed to sustain the IRIS program and database. These factors that have hindered EPA's efforts to improve productivity are

- the OMB/interagency review process managed by OMB,
- the growing complexity and scope of risk assessments,
- certain management decisions and issues regarding the IRIS program,
- congressional action that has delayed some assessments with potentially ~~significant economic effects~~, ~~and~~
- the compounding effect of delays.

OMB/Interagency Review Process

One factor that has made it more difficult for EPA to complete IRIS assessments in a timely manner is the OMB-managed interagency review process, initiated in 2004 at OMB's direction. According to OMB, the purpose of OMB/interagency reviews is to ensure that federal agencies are aware of draft IRIS assessments in which they have an interest and that these agencies have the opportunity to be involved with the IRIS assessments as they are being developed in order to help ensure and increase their quality. This process, initially conducted on an ad hoc basis, was put in place in response to interagency conflicts that EPA faced when it attempted to finalize some IRIS assessments for chemicals that became highly controversial, such as perchlorate, naphthalene, and TCE—chemicals that are or have been considered by some federal agencies, including DOD, DOE, and NASA, to be integral to their missions. Notably, EPA's IRIS assessments of these chemicals could lead to regulatory actions that could, among other things, restrict the use of these chemicals, require agencies to provide protective gear to their employees exposed to the chemicals at work, or require agencies or their contractors to carry out or pay for cleanup of contamination at federal sites. The interagency conflicts about these IRIS assessments have contributed to their delays—

resulting, for example, in EPA having to essentially restart the naphthalene assessment after it had been drafted and peer reviewed.

The OMB/interagency review process has evolved over time, but it remains an informal process with OMB generally communicating its review requirements verbally. OMB has not provided EPA with written guidance, directives, policies, or procedures on this significant review program. In 2005, OMB started requiring EPA to send OMB all draft IRIS assessments for an OMB/interagency review before the assessments are provided to external peer review panels. In addition, OMB requires EPA to send the assessments to OMB a second time, after EPA has addressed the external peer review comments and recommendations. According to EPA officials, in 2007, OMB informed EPA that it cannot send its draft assessments for external peer review or post final EPA assessments on the EPA IRIS database until OMB verbally informs EPA that it has satisfactorily addressed OMB/interagency comments. OMB has not specified which authority or authorities it is using to review IRIS assessments. Because IRIS assessments are not regulations, they are not covered by Executive Order 12866 which provides for OMB review of proposed regulations, among other things. In addition, although in January 2007, Executive Order 13422 amended Executive Order 12866 by establishing a role for OMB in reviewing "significant guidance" documents, which could potentially include IRIS assessments, OMB officials told us that OMB has not formally classified IRIS assessments as significant guidance documents within the meaning of this executive order.[13] These officials said that OMB had the authority to review IRIS assessments prior to the issuance of Executive Order 13422 and was continuing to use this general authority. We note that these executive orders address only OMB's reviews of two specific categories of agency documents and that OMB has not identified IRIS assessments as falling into either of these categories.

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[13] Under the executive order, significant guidance is defined as, "a guidance document disseminated to regulated entities or the general public that may reasonably be anticipated to (1) lead to an annual effect of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities; (2) create a serious inconsistency or otherwise interfere with an action taken or planned by another agency; (3) materially alter the budgetary impacts of entitlements, grants, user fees or loan programs or the rights or obligations of recipients thereof; or (4) raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive order."

Under the OMB/interagency review process for IRIS assessments, OMB identifies the federal agencies from which it will seek comments on the assessments and provides comments and questions to EPA from OMB and the other federal agencies. EPA then revises the assessments to address the comments and questions and also provides OMB with a document discussing how it has addressed each of the issues raised. According to EPA officials, this step is concluded when OMB verbally informs EPA that all of the issues are resolved. Thus, before EPA can provide its draft assessments to external peer reviewers, EPA, OMB, and the other federal agencies must reach agreement on (1) EPA's revised IRIS assessment and (2) the scope of the external peer review, including specific questions reviewers will be asked.

The OMB reviews have primarily been conducted by a policy analyst in the Office of Information and Regulatory Affairs who, according to OMB officials, has a toxicology background and is qualified to conduct these reviews. If EPA does not agree with some of the proposed changes or peer review requirements, OMB officials said the assessment could be elevated to higher management levels within EPA for resolution. Thus, the framework of the OMB/interagency review process can essentially give more weight to OMB and the other federal agencies than to EPA chemical managers who have prepared the assessments and the many scientists and experts who have peer reviewed them. Further, in commenting on OMB's proposed risk assessment bulletin in 2007, the National Academies stated its concern that scientific issues may be superseded by policy considerations to the extent that the technical aspects of risk assessments would be overseen by OMB and not by the peer review process or by agency technical managers. Similarly, an EPA official noted that the farther removed the scientists and experts who have prepared or peer reviewed the assessments are from the negotiations and decisions over assessment changes requested by OMB and other federal agencies, the decisions are based more on political rather than scientific considerations.

According to EPA officials, some of the OMB/interagency reviews have provided valuable input. However, they said the reviews have also added a significant amount of time to the assessment process, in part because the reviews are not subject to any specific time frames or deadlines and because responding to OMB comments in some cases has required several iterations to address nonsubstantive issues involving minor clarifications, semantics, and organization. (We note that according to the executive order under which OMB reviews regulatory actions, OMB must generally complete such reviews within 90 days.) In terms of time frames, our analysis of EPA data as of December 1, 2007, indicate that of the 36 assessments sent to OMB for the first OMB/interagency review, 16 have completed this process. While 4 completed the process in less than 6 months, 12 of them were in the review process for 6 or more months. Moreover, five additional assessments—the previously discussed assessments of acute exposure—were discontinued at the direction of OMB after a year in the OMB/interagency review stage.

In addition, as of December 1, 2007, 5 of 10 draft assessments had completed the second OMB/interagency review, which OMB officials said is conducted by OMB to ensure that EPA has adequately considered the comments from external peer review panels. These assessments were at the second OMB/interagency review stage for periods ranging from 10 days to almost 4 months. According to EPA, while agencies should only point out major scientific issues that would warrant halting the release of the assessment, some comments submitted to them from the second OMB/interagency reviews by OMB have gone beyond their intended purpose of identifying only major scientific concerns and thus have unnecessarily added time to the assessment process. (See app. III for additional information about the time frames for the OMB/interagency reviews.) Further, EPA officials noted that the OMB/interagency review process can delay not only the IRIS assessments undergoing OMB/interagency review but also the other assessments that the EPA chemical managers would be working on or starting if they were not engaged in responding to the OMB/interagency comments.

Overall, the two OMB/interagency reviews managed by OMB have introduced a significant level of uncertainty into the time frames for completing IRIS assessments. This fact was reflected in EPA's December 2005 *Human Health Risk Assessment Multi-Year Plan*, which identified EPA's annual performance goals for fiscal years 2006 through 2012. The goals did not include the number of IRIS assessments completed and posted on the IRIS Web page—the performance goal that would be expected—but instead the number of assessments provided to OMB for the first OMB/interagency review. While EPA's annual performance goal for IRIS assessments had been the number of completed assessments, during the Program Assessment Rating Tool (PART) review by OMB, it was agreed that the number of assessments provided to OMB for OMB/interagency review was the most appropriate annual measure of performance because EPA "relinquishes direct control of production dates" when it sends draft IRIS assessments to OMB.

In addition to adding time to the IRIS assessment process, the OMB/interagency review process also affects the credibility of assessments primarily because the review process lacks transparency. According to EPA's *Risk Characterization Policy and Handbook*, the risk assessment process—which includes the hazard identification and dose-response analysis that constitutes IRIS assessments—should be transparent and its products should be clear, consistent, and reasonable. Transparency is particularly important in cases such as this when potentially affected parties are providing input into, and in some cases questioning, EPA's scientific analyses supporting its IRIS assessments. Specifically, a transparent process allowing IRIS users and the public to see the comments from OMB and other federal agencies—including those potentially impacted by the IRIS assessments—as well as EPA's responses to them, could help alleviate concerns about potential bias in the assessments.

However, under the OMB/interagency review process managed by OMB, the comments EPA receives from OMB and other federal agencies and EPA's responses to them are not available to the public. OMB does not authorize their disclosure to the public on the basis that these communications are internal deliberations of the executive branch. Overall, because the rationale for changes to EPA's scientific assessments stemming from OMB and the interagency review process are not disclosed, the credibility of the IRIS assessments is reduced. We note that the former Assistant Administrator for the Office of Research and Development has emphasized the importance of transparency in the IRIS assessment process. Specifically, he stated that the best cure for controversy surrounding IRIS assessments "is early and frequent visits to the experts, second opinions, and lots of sunshine" (that is, transparency).

Growing Complexity of Risk Assessments and Risk Assessment Methods and Models

Another factor that affects the length of time it takes to complete IRIS assessments is the growing scientific complexity of the assessments. For example, according to John Graham, the former director of both Harvard's Center for Risk Analysis and OMB's Office of Information and Regulatory Affairs, more and different types of scientific data have made the IRIS assessment of health effects more challenging.[14] As a result, EPA chemical managers and scientists need to explore new methods of analyses and evaluate a wider variety of potential health effects (e.g., multiple disease endpoints) than in the past. In addition, chemical managers responsible for the assessments are working with a growing body of complex risk assessment guidelines, such as EPA's 2005 *Guidelines for Carcinogen Risk Assessment* (final revised cancer assessment guidelines) and its supplement relating to children, *Supplemental Guidance for Assessing Susceptibility from Early Life to Exposure to Carcinogens.* In addition, chemical managers must increasingly analyze studies using state-of-the-art physiologically based pharmacokinetic (PBPK) models, which improve the estimation of doses across species and routes of exposure and provide insights on uncertainty.[15] Before EPA relies on PBPK models intended for risk assessments, the agency needs to evaluate them. Such evaluations include a review of the model purpose, structure, mathematical representation, parameter estimation (calibration), and computer implementation. EPA has established criteria for acceptance of a PBPK model for risk assessment purposes in one of two detailed reports issued in 2006, *Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment.* The other 2006 report on PBPK models is the *Use of Physiologically Based Pharmacokinetic (PBPK) Models to Quantify the Impact of Human Age and Interindividual Differences in Physiology and Biochemistry Pertinent to Risk.* In fiscal years 2008 and 2010, EPA plans to issue additional information on PBPK modeling for use in risk assessments.

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[14] Examples cited by the former director include scientific data such as subtle biologic changes, biomarkers, and partial data on one or more mechanistic hypotheses.

The chemical managers are also called upon to use some new methods and models of risk assessment that are being developed or being applied for the first time in the absence of guidelines. For example, uncertainty analysis is a method in the early stages of development and use in risks assessments, for which EPA has not yet developed guidance.[16] However, chemical managers are having to develop and apply new approaches to quantify and communicate uncertainty. According to EPA, these approaches include identifying alternative studies and endpoints for the application of uncertainty factors in noncancer risk assessment and the application of alternative dose-response models for cancer risk assessment. Important cutting-edge assessment models relevant to IRIS assessments include biologically based dose-response models, which are based on the modes of action of chemicals—that is, analysis of physiological, chemical, and biological information that helps identify a chemical agent's role in the development of tumors. These highly complex models can analyze multiple modes of action and can be responsive to EPA's 2005 guidelines for cancer assessment that emphasize mode-of-action evaluation. According to EPA, the agency has extensive experience in qualitative mode-of-action analysis but more limited experience in the quantitative evaluation of multiple modes of action.

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[15] Examples of PBPK model applications in risk assessments include interspecies extrapolation of the dose-response relationship, route-to-route extrapolation, estimation of response from varying exposure conditions, estimation of human variability (within the whole population or subpopulations), and high-to-low dose extrapolation.

[16] EPA plans to release draft reports in 2010 on methods for analyzing and characterizing uncertainty in hazard and dose response and in PBPK models.

EPA Management Decisions and Issues

Some of the IRIS assessment process changes that EPA management has implemented in recent years have made it more difficult for the agency to complete assessments in a timely manner. These changes were aimed primarily at improving the quality of the assessments. It is too early to determine whether or to what extent the changes have enhanced the scientific credibility of the assessments,[17] but it is clear they have contributed to assessment delays overall. Changes that have affected the time frames for IRIS assessments include waiting for additional scientific studies to be completed, waiting for the development of an acceptable methodology for presenting qualitative and quantitative uncertainty analysis in the IRIS assessments, and numerous process changes.

Waiting for additional scientific studies: EPA management's decision in some cases to suspend ongoing IRIS assessments while waiting for additional scientific studies to be completed has contributed to EPA's lack of productivity. According to a former IRIS program director, EPA's general approach in the 1990s was to use only information from completed scientific studies available at the time of the assessment—e.g., the reviews were based on the best available science. However, EPA has awaited the results of new and ongoing studies before completing some IRIS assessments, which has resulted in delaying them for years. Examples of key chemical assessments that have been delayed while EPA waits for new studies include those for formaldehyde and Royal Demolition Explosive,[18] discussed later. Other delayed assessments include those for tetrahydrofuran, perfluorooctane sulfonate-potassium salt (PFOS), and perfluorooctanoic acid-ammonium salt (PFOA). We understand that there may be exceptional circumstances for which it may be appropriate to wait for the results of an important ongoing study, such as a major epidemiological study that will provide new, critical data for an assessment. According to EPA officials, this is the case with research they are awaiting for its IRIS assessment of asbestos. However, as a general rule, requiring that IRIS assessments be based on the best science available at the time of the assessment, as had been the prior practice, is a standard that would best support a goal of completing assessments within reasonable time periods and minimizing the need to conduct significant levels of rework.

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[17] According to an EPA official, the November 2007 review of the IRIS program by the Board of Scientific Counselors, an independent board of experts appointed by EPA to assess its program, concluded that the program "met expectations." A report covering this review, which included evaluating the scientific quality of IRIS assessments, is expected in early 2008.

[18] Also referred to as RDX or hexahydro-1,3,5-trinitrotriazine.

Developing an acceptable uncertainty analysis for IRIS assessments: Another management decision that has delayed the completion of IRIS assessments is to incorporate comprehensive uncertainty analysis into the IRIS assessments. Peer reviews of EPA's assessments by the National Academies and others have sometimes recommended additional uncertainty analysis; the Assistant Administrator, Office of Research and Development, has made the inclusion of qualitative and quantitative uncertainty analyses in IRIS assessments a high priority to, among other things, support better decisions and guide EPA's research agenda. Such analyses require the use of state-of-the-art tools to quantify uncertainty. That is, comprehensive—and, in particular, quantified—uncertainty analysis, is an emerging analytic tool. For example, EPA's August 2007 *Human Health Risk Assessment Multi-Year Plan* estimates releasing an external review draft report on methods for analyzing and characterizing uncertainty in hazard and dose-response assessments in 2010; the plan—which covers 2006 through 2012—does not estimate a final report date for this important guidance on uncertainty analysis. In the interim, EPA chemical managers have had to try to develop complex uncertainty estimates in draft assessments in the absence of agency guidance or protocols. As discussed later, this requirement has delayed the completion of an important assessment (tetrachloroethylene) for almost two years. Moreover, because EPA is now requiring all IRIS assessments to include basic or enhanced uncertainty analysis, other significant assessments that have been drafted have also been delayed, pending approval by the Assistant Administrator, Office of Research and Development, of an acceptable template for uncertainty analysis for significant assessments. Further, external peer reviewers of IRIS assessments containing quantified uncertainty analyses will need to have specialized expertise to assess the quality and reliability of these cutting-edge analyses—which themselves contain uncertainties and incorporate numerous assumptions. Evaluating the uncertainty assessments will be challenging, given their complexities and the lack of guidance on this emerging method. Along these lines, members of the Board of Scientific Counselors[19] have questioned whether expert peer reviewers of EPA's IRIS assessments will have the necessary expertise in this emerging method. Finally, effectively communicating the results of complex uncertainty analyses may be challenging—in fact, some have questioned whether highly detailed quantitative uncertainty analysis enhances the values of risk assessments. For example, in commenting on a proposed OMB bulletin that would have provided risk assessment guidance to federal agencies, the Department of Health and Human Services noted that "characterization of every possible uncertainty or extensive evaluation of each assumption . . . could result in a confusing, less straight-forward document . . . that would not serve the public or the risk assessment community well."[20] Similarly, in its review of the proposed bulletin, the National Academies concluded that "there is a serious danger that agencies will produce ranges of meaningless and confusing risk estimates, which could result in risk assessments of reduced rather than enhanced quality and objectivity."

Continuous process changes, outdated standard operating procedures, and management issues: EPA's continual changes to the IRIS assessment process present a challenge to the chemical managers who are undertaking the assessments. Further, a number of changes have been implemented informally since the last update to the agency's standard operating procedures for fiscal year 2006 reviews. According to EPA, these changes have been made in order to continually improve the assessment process and to respond to changing requirements, such as the OMB-managed OMB/interagency review and the need to incorporate emerging risk assessment methods. Chemical managers have told us that there is much confusion about the process, including who needs to be briefed on the draft assessments and who has approval authority to move an assessment to the next step. In fact, in the absence of current operating procedures to guide chemical managers on basic procedures and program management responsibilities for the development, review, and finalization of IRIS assessments, EPA chemical managers recently took the initiative to develop a detailed graphic providing their best understanding of the process. One aspect of the IRIS assessment process that has become particularly unclear is the steps required to obtain approvals to move draft assessments through various stages (e.g., to OMB, external peer review, or final issuance). For example, until 2004, EPA used an agencywide consensus process to reach either unanimous or substantial agreement on draft assessments among members of the IRIS Agency Review Committee; if agreement could not be reached by the committee, the operating procedures had provided a detailed process for resolving contentious issues. When EPA moved from the consensus approach to an "agency resolution" approach, however, the guidance said only that final decisions on any contentious issues were to be resolved by either the NCEA Director or the Agency Science Advisor.[21] In addition, while approval to move draft assessments to external peer review had been made by the NCEA Director, according to EPA officials, in 2006, the Assistant Administrator started approving drafts for the first of three external reviews of IRIS assessments—the initial OMB/interagency review. However, this change occurred informally and was not reflected in the existing standard operating procedures.[22] We also note that, starting in 2004, chemical managers were required to provide a fact sheet on final IRIS assessments to the Assistant Administrator for review and approval before the assessments could be posted on the Web site.[23] Raising the level at which various approvals are made has added time to the process because it involves additional briefings, additional revisions and negotiations over revisions, and, at times, delays due to scheduling difficulties. As a result, it is important for EPA to both articulate and evaluate its internal review process to help ensure the appropriate balance between product quality and timeliness.

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[19] The Board of Scientific Counselors is a federal advisory committee established by EPA to provide advice, information, and recommendations about the Office of Research and Development's research program.

[20] OMB recently proposed a bulletin that would have provided risk assessment guidance to federal agencies. The proposed bulletin stated that "every quantitative risk assessment should provide a range of plausible risk estimates when there is scientific uncertainty or variability." OMB decided not to finalize the bulletin after a National Academies' committee severely criticized it, noting, among other shortcomings, that "the description of uncertainty and variability in the bulletin is oversimplified and does not recognize the complexities of different types of risk assessments or the need to tailor uncertainty analysis to a given agency's particular needs." In particular, the committee noted that "a central estimate and a risk range might be misleading in situations when sensitive populations are of primary concern." National Academies, *Scientific Review of the Proposed Risk Assessment Bulletin from the Office of Management and Budget Committee to Review the OMB Risk Assessment Bulletin* (Washington, D.C., 2007).

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[21] In January 2006, the Assistant Administrator for Research and Development was appointed as EPA's Science Advisor.

[22] EPA officials said that in July 2007, approval authority to send draft assessments to OMB was again devolved to the Director, NCEA.

[23] According to the fiscal year 2004, 2005, and 2006 standard operating procedures for IRIS assessments, before an assessment is posted on the Web site, chemical managers are required to (1) brief the IRIS Program Director and other NCEA management on any significant changes since external review and (2) prepare a fact sheet for review and approval by the Assistant Administrator, Office of Research and Development, before the IRIS Program Director submits the final assessment documents to the IRIS Web master for posting on the IRIS Web site.

Finally, in addition to process and approval clarifications, it also appears that the IRIS program could benefit from more rigorous management attention and oversight. For example, the risk assessment for chloroform—identified as one of the highest-priority assessments requested by the EPA Office of Air and Radiation—was first announced in a January 1998 *Federal Register* notice; however, the chemical manager for the chloroform assessment retired from the agency in late 2004, and a new chemical manager was not assigned to this assessment until early 2007.[24] Although EPA continued to identify this assessment as ongoing, it was actually unstaffed and therefore suspended for at least 2 years. In addition, a relatively simple, less controversial assessment of 2,2,4-trimethylpentane, which concluded that there were insufficient scientific data to either quantify the noncancer health risks associated with the chemical or to assess its potential to cause cancer, took more than 4 years to complete. EPA officials could not explain why this assessment—which should have taken less than a year to complete—took so long, aside from noting that the responsible staff had been given other high-priority assignments during this time. EPA needs to ensure that its IRIS assessments are given high priority and adequately staffed so that costly delays are avoided.

Congressional Actions

Another factor that can delay the completion of IRIS assessments is the potential for congressional involvement in assessments that become controversial, such as those with potentially significant economic effects. Because of the potential for such assessments to lead to regulatory actions that can significantly affect certain industries or federal agencies, it is particularly important that these assessments effectively and appropriately use the best available science. Even assuming the best available science, however, uncertainties remain an inherent aspect of complex chemical risk assessments. As the National Academies has noted, "A risk assessment usually involves incomplete data, scientific uncertainty, and the need for expert judgment" and "almost every risk assessment is open to challenge on one ground or another."[25] As a result, the assessments may be questioned on various scientific and technical grounds and subjected to intense national scrutiny by many individuals and organizations, including the media. Constituents may contact their elected representatives with their concerns, and politicians are likely to become involved, either supporting the content of the assessments or challenging it. Because of this debate, Members of the Congress, congressional committees, or the Congress as a whole may direct EPA to take certain steps before finalizing a particular assessment. While the intense scrutiny to which some chemical assessments are subjected can result in improved assessments, all uncertainties cannot be eliminated and controversies can continue beyond the point at which additional analysis is helpful. Further, addressing questions and concerns about assessments often involves considerable rework and takes a significant amount of time. EPA strives to balance the desire for the best possible assessment with its responsibilities for protecting the public health~~, which it can only do with timely~~ assessments of chemicals. That being said, it can be challenging for EPA to both identify and achieve the proper balance between these competing goals.

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[24] A December 1998 notice stated that EPA planned to complete the chloroform assessment, as well as 23 other assessments, in fiscal year 1999 or fiscal year 2000. In 2001, EPA completed assessments addressing oral exposure to chloroform (oral RfD and cancer assessments); however, the assessment addressing inhalation exposure (RfC) needed by the Office of Air and Radiation is currently being drafted. Since 2002, EPA has been reporting the chloroform (inhalation route) assessment as being under way or generally complete and planned for entry into IRIS within a year or 2.

In the case of certain controversial chemical assessments, actions by congressional committees and individual members have led EPA to, for example, postpone completion of the IRIS assessment of formaldehyde for years until an update of an epidemiological study that had just been released was completed. Another response to congressional concerns is EPA's decision to reconsider the quantitative noncancer assessment of a chemical, dibutyl phthalate, that had completed all internal and external reviews and was ready to be released in 2007. The noncancer assessment, an update to the assessment completed in 1990, would have allowed more exposure to dibutyl phthalate than the earlier assessment. In 2000, the Department of Health and Human Services' National Toxicology Program concluded that dibutyl phthalate may adversely affect human reproduction or development if exposures are sufficiently high. This chemical, regulated under the Clean Air Act's air toxics program, is used in many consumer products, such as cosmetics, nail polishes, fragrances, wood stains, and toys; the European Union has banned its use in cosmetics and restricted its use in children's toys containing concentrations of phthalates in excess of 0.1 percent. Similarly, after January 1, 2009, a California statute enacted in 2007 will prohibit the manufacture, sale, or distribution of certain toys and child care articles if the products contain concentrations of phthalates exceeding 0.1 percent.[26] Because of congressional questions and comments from the Natural Resources Defense Council about, among other things, the adequacy of the uncertainty factors used in the analysis and the lack of consideration in the draft assessment of cumulative exposure to multiple phthalates (similar chemicals in the same class) that have similar health effects, EPA has suspended the assessment. In December 2007, an EPA official said that EPA has decided to seek advice from the National Academies on whether the agency should develop a new type of assessment for this chemical—one that would assess a class of related chemicals. If EPA decides to develop a new, cumulative IRIS assessment, it will likely be many years before an updated IRIS assessment addressing dibutyl phthalate is completed.[27]

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[25] National Academies, *Scientific Review of the Proposed Risk Assessment Bulletin from the Office of Management and Budget Committee to Review the OMB Risk Assessment Bulletin* (2007).

Compounding Effect of Delays

An overarching factor that affects EPA's ability to complete IRIS assessments in a timely manner is that once a delay in the assessment process occurs, work that has been completed can become outdated, necessitating rework throughout some or all of the assessment process. For example, delays often require repeating reviews of the scientific literature on a chemical to take into account the time that has passed since the literature review was completed; this, in turn, may require detailed analyses of any new studies found to be relevant. Moreover, new risk assessment guidelines and cutting-edge methodologies that the agency has started applying to other assessments may now need to be applied to an assessment being reworked to meet current assessment requirements and standards and the expectations of peer reviewers. Once these analyses are complete, the draft will likely need to be revised and again subjected to internal reviews, OMB/interagency reviews, and scientific peer review. In addition, the longer an assessment is in progress, the more likely it becomes that staff will change due to retirements and resignations; in turn, newly assigned chemical managers face a learning curve in reviewing often voluminous data and analyses. For example, at least four chemical managers have been assigned to the nitrobenzene assessment since it was started in 1998. Overall, even a single delay can have a domino effect—having far-reaching, time-consuming consequences, in some cases, requiring that the assessment process essentially start over. In addition, because chemical managers must continue to devote time and attention to assessments that experience delays—often repeating prior steps to update the assessments—their ability to work on other ongoing assessments and undertake new ones is limited.

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[26] The European Union and California restrictions cover five phthalates, including dibutyl phthalate.

[27] IRIS assessments cover individual chemicals, not cumulative exposure to multiple related chemicals. This is an emerging risk assessment issue that will require developing new assessment methodologies. The congressional letter expressed concerns that the draft IRIS assessment would not adequately protect public health but did not request that it be entirely redone. Among other things, the Natural Resources Defense Council letter suggested that EPA revisit its decisions regarding the uncertainty factors used.

Key IRIS Assessments Have Been Delayed by Some of These Factors

Some key IRIS assessments have been in progress for a number of years, in part because of delays stemming from one or more of the factors discussed above. Examples include the following:

Naphthalene. EPA started the IRIS assessment of cancer risks stemming from the inhalation of naphthalene in 2002. Naphthalene is used in jet fuel and in the production of widely used commercial products such as moth balls, dyes, insecticides, and plasticizers. According to a presentation delivered at the 2007 annual meeting of the Society for Risk Analysis by an Army Corps of Engineers toxicologist,[28] "The changing naphthalene regulatory environment includes a draft EPA risk assessment that if/when finalized, will change naphthalene's status from 'possible' to 'likely' human carcinogen."[29] Thus, according to this presentation, one potential impact of this IRIS assessment on DOD is that DOD would need to provide many employees exposed to naphthalene with equipment measuring their exposure to the chemical. In addition, because many military bases are contaminated with naphthalene, a component of jet fuel (approximately 1 percent to 3 percent) used by all DOD services, DOD could face extensive cleanup costs. By 2004, 2 years after starting the assessment, EPA had drafted a chemical assessment that had completed internal peer reviews and was about to be sent to an external peer review committee. Once it returned from external review, the next step, at that time, would have been a formal review by EPA's IRIS Agency Review Committee. If approved, the assessment would have been completed and released. However, in part because of concerns raised by DOD, OMB asked to review the assessment and conducted an interagency review of the draft. In their 2004 reviews of the draft IRIS assessment, both OMB and DOD raised a number of concerns about the assessment and suggested to EPA that it be suspended until additional research could be completed to address what they considered to be significant uncertainties associated with the assessment. Although all of the issues raised by OMB and DOD were not resolved, EPA continued with its assessment by submitting the draft for external peer review, which was completed in September 2004.[30] However, according to EPA, OMB continued to object to the draft IRIS assessment and directed EPA to convene an additional expert review panel on genotoxicity to obtain recommendations about short-term tests that OMB thought could be done quickly.[31] According to EPA, this added 6 months to the process, and the panel, which met in April 2005, concluded that the research that OMB was proposing could not be conducted in the short term. Nonetheless, EPA officials said that the second expert panel review did not eliminate OMB's concerns regarding the assessment, which they described as reaching a stalemate. In September 2006, EPA decided, however, to proceed with developing the assessment. By this time, the naphthalene assessment had been in progress for over 4 years; EPA decided that the IRIS noncancer assessment, issued in 1998, was outdated and needed to be revisited. Thus, EPA expanded the IRIS naphthalene assessment to include both noncancer and cancer assessments. As a result, 6 years after the naphthalene assessment began, it is now back at the drafting stage. The assessment now will need to reflect relevant research completed since the draft underwent initial external peer review in 2004, and it will have to undergo all of the IRIS assessment steps again, including additional internal and external reviews that are now required. This series of delays has limited EPA's ability to conduct its mission. For example, the Office of Air and Radiation has identified the naphthalene assessment as one of its highest-priority needs for its air toxics program. In addition, the Office of Solid Waste and Emergency Response considers the naphthalene assessment a high priority for the Superfund program—naphthalene has been found in at least 654 of Superfund's current or former National Priorities List sites.[32] Although EPA currently estimates that it will complete the assessment in 2009, meeting this revised estimate will be challenging, given all of the steps that are yet to be completed and the extensive external scrutiny to which it will continue to be subjected.

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[28] Presentations at the Society for Risk Analysis meting reflect the views of the authors and "do not necessarily reflect the views of any other organization or agency."

[29] Using its 1996 Proposed Guidelines for Carcinogen Risk Assessment, EPA concluded in the 1998 IRIS assessment of naphthalene that its human carcinogenic potential could not be determined at that time, but noted that there was suggestive evidence of potential human carcinogenicity. (EPA also noted that under its 1986 cancer guidelines, EPA classified naphthalene as a possible human carcinogen.) Subsequently, in 2002, the International Agency for Research on Cancer (IARC), part of the World Health Organization, concluded that naphthalene is possibly carcinogenic to humans; in 2004, the Department of Human Health and Services' National Toxicology Program concluded that naphthalene can reasonably be anticipated to be a human carcinogen. EPA's current assessment will be subject to the agency's 2005 cancer guidelines.

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[30] According to DOD, EPA did not specifically ask the peer reviewers to address some of the technical questions DOD had raised and wanted the peer review to address.

[31] Genotoxic substances are a type of carcinogen, specifically those capable of causing genetic mutation and of contributing to the development of tumors. This includes both certain chemical compounds and certain types of radiation.

Royal Demolition Explosive. This chemical, also called RDX or hexahydro-1,3,5-trinitrotriazine, is a highly powerful explosive used by the U.S. military in thousands of munitions. Currently classified by EPA as a possible human carcinogen, this chemical is known to leach from soil to groundwater. Royal Demolition Explosive can cause seizures in humans and animals when large amounts are inhaled or ingested, but the effects of long-term, low-level exposure on the nervous system are unknown. As is the case with naphthalene, the IRIS assessment could potentially require DOD to undertake a number of actions, including steps to protect its employees from the effects of this chemical and to clean up many contaminated sites. Although EPA started an IRIS assessment of Royal Demolition Explosive in 2000, it has made minimal progress on the assessment because EPA agreed to a request by DOD to wait for the results of DOD-sponsored research on this chemical. In 2007, EPA began to actively work on this assessment, although some of the DOD-sponsored research is still outstanding.

Formaldehyde. EPA began an IRIS assessment of formaldehyde in 1997 because the existing assessment was determined to be outdated.[33] Formaldehyde is a colorless, flammable, strong-smelling gas used to manufacture building materials, such as pressed wood products, and used in many household products, including paper, pharmaceuticals, and leather goods. While EPA currently classifies formaldehyde as a probable human carcinogen, the International Agency for Research on Cancer (IARC), part of the World Health Organization, classifies formaldehyde as a known human carcinogen. Since 1986, studies of industrial of workers have suggested that formaldehyde exposure is associated with nasopharyngeal cancer, and possibly with leukemia. For example, in 2003 and 2004, the National Cancer Institute (NCI) and the National Institute of Occupational Safety and Health (NIOSH) released epidemiological studies following up on earlier studies tracking about 26,000 and 11,000 industrial workers, respectively, exposed to formaldehyde; the updates showed exposure to formaldehyde might also cause leukemia in humans, in addition to the cancer types previously identified. According to NCI officials, the key findings in their follow-up study were an increase in leukemia deaths and, more significantly, an exposure/response relationship between formaldehyde and leukemia—as exposure increased, the incidence of leukemia also rose. As with the earlier study, NCI found more cases of a rare form of cancer, nasopharyngeal cancer, than would usually be expected. The studies from NCI and NIOSH were published in 2003 and 2004,[34] around the time that EPA was still drafting its IRIS assessment. In November 2004, the Chairman of the Senate Environment and Public Works Committee requested that EPA delay completion of its IRIS assessment until an update to the just-released NCI study could be conducted, indicating that the effort would take, at most, 18 months. EPA agreed to wait—and more than 3 years later, the NCI update is not yet complete. As of December 2007, NCI estimates that the study will be completed in two stages, one in mid-2008 and the second one later that year. An NCI official said that the additional leukemia deaths identified in the update provide "greater power" to detect associations between exposure to formaldehyde and cancer. EPA's inability to complete the IRIS assessment it started more than 10 years ago in a timely manner has had a significant impact on EPA's air toxics program. Specifically, when EPA promulgated a national emissions standard for hazardous air pollutants covering facilities in the plywood and composite wood industries in 2004, EPA's Office of Air and Radiation took the unusual step of not using the existing IRIS estimate but rather decided to use a cancer risk estimate developed by an industry-funded organization, the CIIT Centers for Health Research (formerly, the Chemical Industry Institute of Toxicology) that had been used by the Canadian health protection agency. The IRIS cancer risk factor had been subject to criticism because it was last revised in 1991 and was based on data from the 1980s. In its final rule, EPA stated that "the dose-response value in IRIS is based on a 1987 study, and no longer represents the best available science in the peer-reviewed literature." The CIIT quantitative cancer risk estimate that EPA used in its health risk assessment in the plywood and composite wood national emissions standard indicates a potency about 2,400 times lower than the estimate in IRIS that was being re-evaluated and that did not yet consider the 2003 and 2004 NCI and NIOSH epidemiological studies. According to an EPA official, an IRIS cancer risk factor based on the 2003 and 2004 NCI and NIOSH studies would likely be close to the current IRIS assessment, which EPA has been attempting to update since 1997. The decision to use the CIIT assessment in the plywood national emissions standard was controversial, and officials in EPA's National Center for Environmental Assessment said the center identified numerous problems with the CIIT estimate. Nonetheless, the Office of Air and Radiation used the CIIT value, and that decision was a factor in EPA exempting certain facilities with formaldehyde emissions from the national emissions standard. In June 2007, a federal appellate court struck down the rule, holding that EPA's decision to exempt certain facilities that EPA asserted presented a low health risk exceeded the agency's authority under the Clean Air Act.[35] Further, the continued delays of the IRIS assessment of formaldehyde—currently estimated to be completed in 2010 but after almost 11 years still in the draft development stage—will impact the quality of other EPA regulatory actions, including other air toxics rules and requirements.

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[32] The National Priorities List is EPA's list of seriously contaminated sites.

[33] The cancer portion of the formaldehyde assessment was originally issued in 1989 and updated in 1991; the noncancer assessment was added in 1990.

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[34] NCI published the results of its study in two publications. The first study, published in November 2003, focused on the association between formaldehyde exposure and leukemia. M. Hauptmann, J. H. Lubin, P. A. Stewart, R. B. Hayes, A. Blair, "Mortality from Lymphohematopoietic Malignancies among Workers in Formaldehyde Industries," *Journal of the National Cancer Institute* (2003). The second study, published in June 2004, evaluated the association between formaldehyde exposure and other cancers—including nasopharyngeal cancer. M. Hauptmann, J. H. Lubin, P. A. Stewart, R. B. Hayes, A. Blair, "Mortality from Solid Cancers among Workers in Formaldehyde Industries," *American Journal of Epidemiology* (2004). The results of the NIOSH study were described in one publication, dated March 2004, which assessed mortality from all causes and all cancers. L. E. Pinkerton, M. J. Hein, L. T. Stayner, "Mortality among a Cohort of Garment Workers Exposed to Formaldehyde: an Update," *Occupational and Environmental Medicine* (2004).

Trichloroethylene. Also known as TCE, this chemical is a solvent widely used as a degreasing agent in industrial and manufacturing settings; it is a common environmental contaminant in air, soil, surface water, and groundwater. TCE has been linked to cancer, including childhood cancer, and other significant health hazards, such as birth defects. TCE is the most frequently reported organic contaminant in groundwater, and contaminated drinking water has been found at Camp Lejeune, a large Marine Corps base in North Carolina. TCE has also been found at Superfund sites and at many industrial and government facilities, including aircraft and spacecraft manufacturing operations. In 1995, the International Agency for Research on Cancer classified TCE as a probable human carcinogen, and in 2000, the Department of Health and Human Services' National Toxicology Program concluded that it is reasonably anticipated to be a human carcinogen. Because of questions raised by peer reviewers about the IRIS cancer assessment for TCE, EPA withdrew it from IRIS in 1989 but did not initiate a new TCE cancer assessment until 1998. In 2001, EPA issued a draft IRIS assessment for TCE that proposed a range of toxicity values indicating a higher potency than in the prior IRIS values and characterizing TCE as "highly likely to produce cancer in humans." The draft assessment, which became controversial, was peer reviewed by EPA's Scientific Advisory Board and released for public comment. A number of scientific issues were raised during the course of these reviews, including how EPA had applied emerging risk assessment methods—such as assessing cumulative effects (of TCE and its metabolites) and using a physiologically based pharmacokinetic model—and the uncertainty associated with the new methods themselves.[36] To help address these issues, EPA, DOD, DOE, and NASA sponsored a National Academies review to provide guidance. The National Academies report, which was issued in 2006, concluded that the weight of evidence of cancer and other health risks from TCE exposure had strengthened since 2001 and recommended that the risk assessment be finalized with currently available data so that risk management decisions could be made expeditiously. The report specifically noted that while some additional information would allow for more precise estimates of risk, this information was not necessary for developing a credible risk assessment. Nonetheless, 10 years after EPA started its IRIS assessment, the TCE assessment is back at the draft development stage. EPA estimates this assessment will be finalized in 2010. More in line with the National Academies' recommendation to act expeditiously, five senators introduced a bill in August 2007 that, among other things, would require EPA to both establish IRIS values for TCE and issue final drinking water standards for this contaminant within 18 months.

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[35] *Natural Resources Defense Council v. E.P.A.*, 489 F.3d 1364, 1372-73 (D.C. Cir, 2007). The court did not specifically address EPA's reliance on the CIIT study, holding instead that the Clean Air Act prohibited establishment of the exemptions at issue.

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[36] Physiologically based pharmacokinetic models are a class of dosimetry models that are useful for predicting internal doses to target organs. With the appropriate data, these models can be used to extrapolate across species and exposure scenarios and address various sources of uncertainty in risk assessments.

Tetrachloroethylene. EPA started an IRIS assessment of tetrachloroethylene—also called perchloroethylene or "perc"—in 1998. Tetrachloroethylene is a manufactured chemical widely used for dry cleaning of fabrics, metal degreasing, and making some consumer products and other chemicals. Tetrachloroethylene is a widespread groundwater contaminant, and the Department of Health and Human Services' National Toxicology Program has determined that it is reasonably anticipated to be a carcinogen. The IRIS database currently contains a 1988 noncancer assessment based on oral exposure that will be updated in the ongoing assessment. Importantly, the ongoing assessment will also provide a noncancer inhalation risk and a cancer assessment. The IRIS agency review of the draft assessment was completed in February 2005, the draft assessment was sent to OMB for OMB/interagency review in September 2005, and the OMB/interagency review was completed in March 2006. EPA had determined to have the next step, external peer review, conducted by the National Academies—the peer review choice reserved for chemical assessments that are particularly significant or controversial. EPA contracted with the National Academies for a review by an expert panel, and the review was scheduled to start in June 2006 and be completed in 15 months. However, as of December 2007, the draft assessment has not yet been provided to the National Academies. After verbally agreeing with both the noncancer and cancer assessments following briefings on the assessments, the Assistant Administrator, Office of Research and Development, subsequently requested that additional uncertainty analyses—including some quantitative analyses—be conducted and included in the assessment before the draft was released to the National Academies for peer review. As discussed above, quantitative uncertainty analysis is a risk assessment tool that is currently being developed, and although the agency is working on developing policies and procedures for uncertainty analysis, such guidance currently does not exist. The draft tetrachloroethylene assessment has been delayed since early 2006 as EPA staff have gone back and forth with the Assistant Administrator trying to reach agreement on key issues such as whether a linear or nonlinear model is most appropriate for the cancer assessment and how uncertainty should be qualitatively and quantitatively characterized. EPA officials and staff noted that some of the most experienced staff are being used for these efforts, limiting their ability to work on other IRIS assessments. In addition, the significant delay has impacted the planned National Academies peer review because the current contract, which has already been extended once, cannot be extended beyond December 2008. The peer review was initially estimated to take 15 months. As a result, a new contract and the appointment of another panel may be required.

Dioxin. The dioxin assessment is an example of an IRIS assessment that has been, and will likely continue to be, a political as well as a scientific issue. Often the byproducts of combustion and other industrial processes, complex mixtures of dioxins enter the food chain and human diet through emissions into the air that settle on soil, plants, and water. EPA's initial dioxin assessment, published in 1985, focused on the dioxin TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) because animal studies in the 1970s showed it to be the most potent cancer-causing chemical studied to date. Several years later, EPA decided to conduct a reassessment of dioxin because of major advances that had occurred in the scientific understanding of dioxin toxicity and significant new studies on dioxins' potential adverse health effects. Initially started in 1991, this assessment has involved repeated literature searches and peer reviews. For example, a draft of the updated assessment was reviewed by a scientific peer review panel in 1995, and three panels reviewed key segments of later versions of the draft in 1997 and 2000. In 2002, EPA officials said that the assessment would conclude that dioxin may adversely affect human health at lower exposure levels than had previously been thought and that most exposure to dioxins occurs from eating such American dietary staples as meats, fish, and dairy products, which contain minute traces of dioxins. These foods contain dioxins because animals eat plants and commercial feed and drink water contaminated with dioxins, which then accumulate in animals' fatty tissue. It is clear that EPA's dioxin risk assessment could have a potentially significant impact on consumers and on the food and agriculture industries. As EPA moved closer to finalizing the assessment, in 2003 the agency was directed in a congressional appropriations conference committee report to not issue the assessment until it had been reviewed by the National Academies. The National Academies provided EPA with a report in July 2006. In developing a response to the report, which the agency is currently doing, EPA must include new studies and risk assessment approaches that did not exist when the assessment was drafted. EPA officials said the assessment will be subject to the IRIS review process once its response to the National Academies' report is drafted. As of 2008, EPA has been developing the dioxin assessment, which has potentially significant health implications for all Americans, for 17 years.

While Appropriate Coordination with Federal Agencies Could Help EPA Resolve IRIS Assessment Controversies More Efficiently, EPA's Proposed Expansion of Agencies' Roles in IRIS Assessments Would Cause Further Delays and Limit Their Credibility

Although an interagency review process managed by OMB was informally incorporated into the IRIS assessment starting in 2004, federal agencies continue to believe they should have greater and more formal roles in EPA's development of IRIS assessments given the potential impact of the assessments on either their missions or their budgets, such as the need to redesign systems to eliminate hazardous materials or to clean up contaminated sites. These agencies—including DOD, DOE, the Department of Homeland Security, the Department of Transportation, and NASA—have sought earlier, more formal involvement in IRIS assessments than is currently provided through the OMB/interagency review process and the other avenues for input that currently exist, which include nominating chemicals for assessment and providing relevant studies for planned or ongoing assessments. Officials from DOD, NASA, and DOE told us there is a lack of formality and transparency about how they can provide input and when it is appropriate to do so. For example, they seek a more formal process for nominating chemicals and providing relevant studies for planned or ongoing assessments, and they want to help decide questions for the peer reviews of IRIS assessments. They said that reducing the scientific uncertainty in IRIS assessments is important because some assessments can have significant impacts on their operations and budgets. Also, the officials said that their involvement with IRIS assessments occurs too late in the process, leading to disagreement among EPA and the agencies after the assessments are drafted, and unnecessarily delaying certain assessments, such as naphthalene, TCE, and dioxin.

Along these lines, we concluded in a 2006 report that EPA could help ensure consistent, transparent, and high-quality risk assessments by working with stakeholders early and periodically throughout the process to identify, among other things, key issues and studies that need to be considered in the analysis.[37] Nonetheless, we believe that if EPA is to increase the involvement of DOD and other potentially affected federal agencies in the IRIS assessment process, it is important to do so in a way that enables EPA to balance the benefits of increased interagency coordination with EPA's need to improve the timeliness of its IRIS assessments and to ensure their credibility with proper controls.

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[37] GAO, *Human Health Risk Assessment: EPA Has Taken Steps to Strengthen Its Process, but Improvements Needed in Planning, Data Development, and Training,* GAO-06-595 (Washington, D.C.: May 31, 2006).

In response to the continuing concerns of some federal agencies regarding the IRIS assessment process, EPA has, for several years, been working to develop a formal IRIS assessment process that would give other federal agencies a more significant role in the process.[38] EPA consulted with an Interagency Work Group on the IRIS Process, which includes officials representing potentially affected agencies such as DOD, DOE, and NASA, as well as officials from other agencies that develop health assessments of chemicals, such as the Department of Health and Human Services' ATSDR. OMB, the Department of Homeland Security, and the White House Office of Science and Technology Policy are also represented on the working group.

EPA developed a draft process in early 2007 that the agency believed would be acceptable to the interagency work group. One of the key aspects of EPA's draft process is an increased role for other agencies—including those whose operations and resource levels could be affected by the results of the assessments—in providing input to IRIS chemical assessments. Specifically, federal agencies would have the opportunity to be involved, or provide some form of input, at almost every step of EPA's IRIS assessment process. Most significantly, the draft proposed process would provide federal agencies with several opportunities during the IRIS assessment process to identify chemicals of interest to them as "mission critical." As defined in the draft process, a mission-critical chemical is one that is "an integral component to the successful and safe conduct of an agency's mission in any or all phases of operations." Potential impacts on the use of mission-critical chemicals assessed under the IRIS program include "cessation or degradation of the conduct of the mission and/or unacceptable resource constraints."[39] A mission-critical designation would add requirements to the assessment process, providing other federal agencies with increased involvement in IRIS assessment decisions. As outlined, this designation could add 2 or more years to the process (see shaded boxes in fig. 5 for these additional requirements).

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[38] Developing this process, publishing a notice about it in the *Federal Register*, and holding a public meeting to obtain public input on the proposed process has been an item OMB has included in its PART review of EPA's human health risk assessment program.

[39] Under the proposal, EPA could also identify chemicals "of major importance" which would be treated as mission-critical chemicals.

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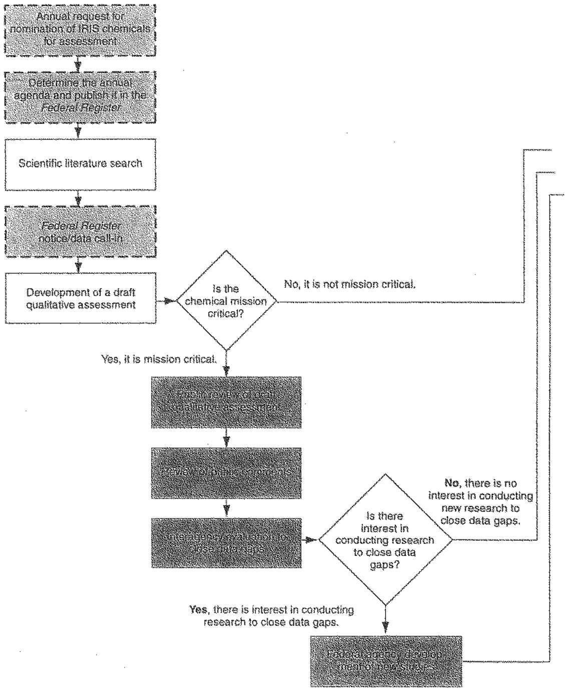
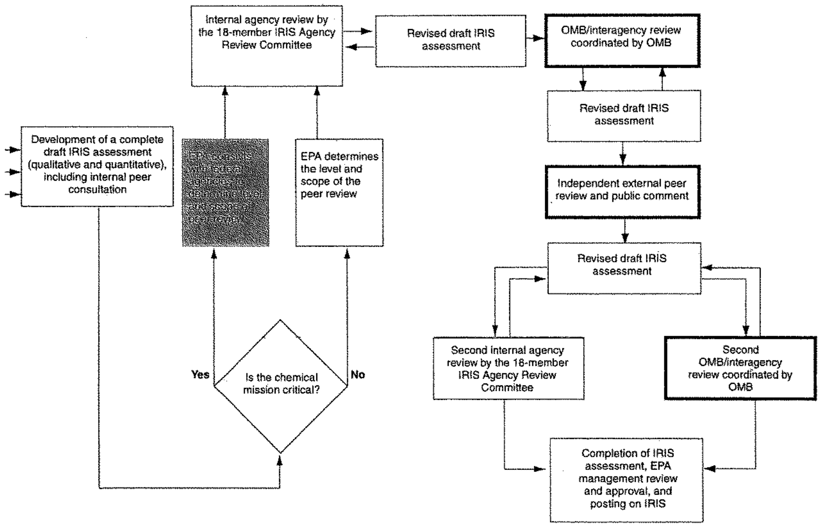
Figure 5: EPA's Draft Proposed IRIS Assessment Process


Annual request for nomination of IRIS chemicals for assessment
Determine the annual agenda and publish it in the *Federal Register*
Scientific literature search
Federal Register notice/data call-in
Development of a draft qualitative assessment
Is the chemical mission critical?
No, it is not mission critical.
Yes, it is mission critical.
Public review of draft qualitative assessment
Review of public comments
Interagency evaluation to close data gaps
Is there interest in conducting research to close data gaps?
No, there is no interest in conducting new research to close data gaps.
Yes, there is interest in conducting research to close data gaps.
Federal agency development of new studies


Internal agency review by the 18-member IRIS Agency Review Committee
Revised draft IRIS assessment
OMB/interagency review coordinated by OMB
Revised draft IRIS assessment
Development of a complete draft IRIS assessment (qualitative and quantitative), including internal peer consultation
EPA consults with federal agencies to determine level and scope of peer review
EPA determines the level and scope of the peer review
Independent external peer review and public comment
Revised draft IRIS assessment
Yes
Is the chemical mission critical?
No
Second internal agency review by the 18-member IRIS Agency Review Committee
Second OMB/interagency review coordinated by OMB
Completion of IRIS assessment, EPA management review and approval, and posting on IRIS

■ Darker shaded boxes are additional steps, under EPA's planned changes, to its assessment process and indicate steps where EPA has provided additional opportunity for input from potentially affected federal agencies for mission-critical chemicals.

▨ Lighter shaded boxes with dotted lines indicate steps where EPA has provided additional opportunity for input from potentially affected federal agencies for all chemicals.

☐ White boxes with heavy lines indicate steps where potentially affected federal agencies already had an opportunity for input.

Source: GAO analysis of EPA information.

The additional requirements for assessments of mission-critical chemicals that would lengthen the IRIS assessment process include the following:

- *The opportunity for federal agencies and the public to identify any additional information that is available on a chemical and to correct any errors on EPA's new first assessment draft—a draft qualitative assessment.*[40] EPA estimates that the public comment period alone would add 45 days to the assessment process.
- *An opportunity for potentially affected federal agencies to review public comments made during the error correction step and initiate a meeting with EPA if they want to discuss a particular set of comments.* EPA estimates that this step, which includes EPA's review and analysis of the public comments, would add 30 days to the process.
- *An opportunity for potentially affected federal agencies to fill a data gap or eliminate an uncertainty factor that is identified in the qualitative draft.* If an agency believes it can sponsor research to fill a significant data gap, EPA would then suspend the assessment process for up to 18 months to allow that agency time to conduct research and have the completed study peer reviewed.

In addition, the draft proposed process would give other federal agencies a formal role in helping EPA determine the level of independent peer review assessments for mission-critical chemicals—that is, whether the peer reviews would be conducted by EPA Science Advisory Board panels, National Academies' panels, or panels organized by an EPA contractor. In addition, the other federal agencies would be able to help determine the panel members' areas of scientific expertise as well as the scope of the peer reviews and the specific issues they would address.

Finally, the draft proposed process would also formalize the roles of other federal agencies in nominating chemicals for assessment, helping EPA determine the chemicals it would assess, and providing scientific information (reports, studies, etc.) for the assessments EPA undertakes. In the past, EPA sought such information in public notices in the *Federal Register*, and federal agencies could have provided their input either in response to these notices or by contacting EPA officials directly. However, in response to criticisms that EPA's approach to seeking input from the public was not appropriate for other federal agencies, under the proposed process, EPA would directly reach out to other federal agencies for this input by separately communicating these requests to them at the time it publishes its notices in the *Federal Register*. The draft proposed IRIS process would also formalize the OMB/interagency reviews, which provide other federal agencies with the opportunity to provide comments on IRIS draft assessments both before and after the draft assessments are provided to external peer reviewers. The OMB/interagency reviews would continue to be managed by OMB.

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[40] Under EPA's draft proposed IRIS assessment process, EPA would develop, for all chemicals, an additional draft IRIS assessment—one that includes only qualitative information—that must undergo internal review. Only draft qualitative assessments for chemicals that are identified as mission critical would be released for the error correction step.

EPA has acknowledged that the additional steps and opportunities for input from other federal agencies that its draft proposed process would provide will add more time to an already lengthy process. Specifically, under the proposed process we reviewed, EPA officials estimated that IRIS assessments for standard chemicals would take roughly 2-1/2 years to complete and that an additional 2 to 3 years would be needed for mission-critical chemicals. In February 2008, the Assistant Administrator, Office of Research and Development, updated these time frames, estimating that most assessments would take between 3 and 4-1/2 years to complete, while assessments of mission-critical chemicals would take up to 6 years. However, these estimates appear to be optimistic considering the length of time ongoing assessments—which have not been subject to additional process steps—have been in progress: most for more than 5 years and many for more than 9 years. Further, when assessments take longer than 2 years, they can become subject to substantial delays stemming from the need to redo key analyses to take into account changing science and assessment methodologies.

According to officials from EPA and some of the potentially affected federal agencies, the key goals of the draft proposed changes to the IRIS assessment process are to (1) fill data gaps to reduce uncertainty in the IRIS assessments and (2) prevent disagreements among EPA and other federal agencies about assessments late in the IRIS assessment process. As discussed earlier, disagreements have arisen late in the process in the past and have significantly delayed the completion of some assessments. These goals are important, and it is appropriate for EPA and the federal agencies to find ways to achieve them. However, some of the proposed changes would result in assessments being caught in a continuous cycle of updates and revisions—delaying the completion of assessments of chemicals with potentially significant health impacts for many years. As discussed above, delays for any reason—including waiting for new research to fill data gaps—can have a compounding effect on time frames because delays often require extensive rework, such as updates to reflect other studies that have come out in the interim, performing additional analyses to reflect the current state of the science of risk assessment tools, and other rounds of interagency or external peer reviews because of changes in the assessments. Thus, changing from a reliance on the best available scientific data at the time an assessment is conducted to a reliance on research that has either not yet started or been completed in order to fill scientific data gaps is a decision that can have a significant impact on assessment completion dates.

Further, although EPA has said that IRIS assessments would only be suspended to wait for shorter-term studies, such as those assessing modes of action, we and several agency officials we spoke with believe that the time needed to plan, conduct, and complete research that would address significant data gaps, and have it peer reviewed, would likely take longer than the 18 months EPA would allow under its draft proposed IRIS process. In addition, although the draft process would set a limit on the time the assessments can be suspended to await studies, the enforcement of such time frames could prove to be difficult when research schedules slip. And not waiting for study results beyond the 18-month limit could, in fact, undo all of the efforts expended to avoid disagreements in the later stages of the assessments. Also, EPA's prior experience with waiting for studies, such as in the case of the formaldehyde assessment discussed earlier, shows that estimates of completion dates for these studies can stretch out from months to years. Finally, the extent to which new research would provide information that would actually reduce key scientific uncertainties in the IRIS assessments is not known until the research is completed and peer reviewed.

In discussing with us the need for additional time to conduct new research to fill scientific data gaps for chemicals defined as mission critical, DOD officials emphasized that the federal agencies believe it is important that scientific uncertainties are reduced to the maximum extent practical within a reasonable time frame before IRIS assessments of mission-critical chemicals with high uncertainty are completed. The potential impacts of IRIS assessments on DOD—should risk assessments using the IRIS data lead to regulatory actions—could include the need to (1) conduct research and development of material substitutes; (2) redesign systems and processes to eliminate hazardous materials; (3) conduct research and development of treatment or cleanup technologies; (4) improve personal protective clothing, equipment, and procedures; and (5) provide for special handling and storage of chemicals.

However, the reality is that scientific data gaps will almost always exist. EPA, whose mission includes protecting the public and the environment from harmful chemicals, must decide whether to use assumptions and estimates to address data gaps or to wait for research that could potentially fill some of the data gaps. On this issue, in discussing the fact that EPA must address many environmental risks with incomplete data and a lack of consensus about assumptions, the agency has stated that it seeks to strike a balance among fairness, accuracy, and efficient action because not acting until data quality improves can result in substantial harm to human health, safety, and the environment. Along these lines, as discussed earlier, a National Academies panel recently reported on a chemical of interest (trichloroethylene) to several federal agencies that would likely be defined as mission critical under the proposed IRIS process. The National Academies' report recommended that the risk assessment be finalized with currently available data, rather than waiting for additional information to address scientific uncertainties, so that risk management decisions can be made expeditiously because the evidence on risks to human health have strengthened. The National Academies specifically noted that while some additional information would allow for more precise estimates of risk, this information is not necessary at this time for developing a credible risk assessment. EPA started the assessment in 1998, and it has been subject to multiple independent peer reviews. However, EPA is currently preparing another assessment draft that will need to undergo the IRIS assessment process a second time. As such, the draft will be to subject to the OMB/interagency reviews and another independent peer review before it can be finalized. We note that if EPA's proposed IRIS process is implemented, DOD and other federal agencies could designate trichloroethylene as a mission-critical chemical and have the assessment suspended for 18 months for research aimed at reducing scientific uncertainties.

EPA could potentially minimize or eliminate requests to suspend ongoing assessments to fill in scientific data gaps by better coordinating with DOD's emerging contaminants program—established in 2006—that leads and supports the Materials of Emerging Regulatory Interest Team (MERIT).[41] The intent of the emerging contaminants program is to help DOD proactively manage chemicals DOD uses or has used in its operations that (1) are a perceived or real threat to human health or the environment and (2) lack a published health standard and/or have new information available about their sources or effects. The program seeks to identify chemicals of importance to DOD's mission that are on the regulatory horizon so that the agency can begin to make changes or identify areas of research that may minimize the impact that regulations of a particular chemical would have on the agency and its mission.

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[41] According to DOD, the Materials of Emerging Regulatory Interest Team is a virtual interagency team composed of individuals throughout DOD with a common interest in emerging contaminants.

Of particular relevance to the IRIS program is the scanning component of the emerging contaminants program, which consists of a regular review of the scientific literature, periodicals, and regulatory communications for chemicals that have, or are likely to have, changing human health values or regulatory standards. DOD then further screens those chemicals that are, were, or will be used by DOD to determine whether a potential impact to DOD's mission exists. After screening, DOD conducts impact assessments to determine the severity of risk to DOD functional areas, which include environment, safety, and health protection; research and development; production, operation and maintenance, and disposal; training and readiness; and cleanup. Through these efforts, DOD seeks to identify cost-effective opportunities to proactively manage future unacceptable risks. One research area the emerging contaminants program has identified as a potentially good investment is DOD-funded health effects research aimed at filling important data gaps for mission-critical chemicals with high uncertainty factors.[42]

DOD's ongoing actions in monitoring scientific literature and identifying research that could reduce scientific uncertainties could be more effectively put to use. Specifically, enhanced coordination and collaboration between EPA and DOD's emerging contaminants program have the potential to proactively reduce some scientific uncertainties associated with chemicals that EPA is not yet assessing—as opposed to the current reactive focus on ongoing IRIS assessments. That is, under the draft proposed IRIS process changes we reviewed, DOD and other federal agencies would be able to designate ongoing chemicals as mission critical at several stages in the assessment process—and have their assessments suspended for up to 18 months to address data gaps. However, enhanced coordination and collaboration between DOD and EPA could change this essentially reactive approach to a model that is more proactive and effective. If, for example, EPA provided 2 years' notice of its intent to assess specific chemicals, rather than simply announcing the list of chemical assessments it plans to initiate during a given fiscal year, DOD and other agencies could use this time to sponsor and complete the studies they deem necessary, rather than waiting to initiate them after an IRIS assessment had started. Giving agencies 2 years' notice (which would provide them with more than 18 months to conduct additional research) would be more effective and efficient than delaying ongoing IRIS assessments for 18 months to await research, given the compounding effect of delays on IRIS assessments. We note that, to date, the emerging contaminants action list—the list of chemicals that DOD has assessed and judged to have a significant potential impact on people or the DOD mission—has focused largely on chemicals that EPA's IRIS program is already assessing. However, with some adjustments in the emerging contaminants program's focus or scope, DOD could widen its scope and help EPA with its planning process by earlier identification of the mission-critical chemicals of concern to DOD for which IRIS assessments are needed. Finally, when the emerging contaminants program identifies health research needs for chemicals considered mission critical, DOD could meet its research needs more effectively and quickly by sponsoring research as needs are identified, rather than waiting until IRIS assessments are started.

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[42] Other possible types of DOD risk management investments include material and process substitutions and personal protective equipment.

Lastly, we note that while increased coordination with potentially affected federal agencies on IRIS assessments could enhance the assessments and facilitate their completion, giving potentially affected federal agencies formal roles in some IRIS assessment decisions reduces the credibility of the assessments if proper controls, such as ensuring transparency, are not in place. While we recommended in our 2006 report on human health risk assessment that EPA consistently involve stakeholders as appropriate to the risk assessment, we made this recommendation in the context of improving the overall quality, consistency, and transparency of risk assessments. However, one aspect of EPA's draft proposed IRIS process that has proven to be controversial involves transparency. Specifically, EPA's early 2007 draft proposal included making the comments from OMB and other federal agencies provided during the OMB/interagency review process part of the public record; according to EPA, this requirement has been removed from the latest draft proposal because of concerns raised by OMB. These concerns have delayed the implementation of the planned process changes, and as of December 2007, EPA was planning to send a revised draft back to the interagency work group for review and approval.

According to DOD officials, OMB did not support certain aspects of the draft process EPA presented to the Interagency Work Group on the IRIS Process in early 2007, expressing concerns about how the proposal would address the concerns of states, industry, and environmental entities and the requirement to have agencies' comments part of the public record. The latter concern stemmed from the precedent it might set and because OMB believes that doing so would erode the effectiveness of the deliberative process among EPA and the agencies. However, because the agencies' comments on IRIS assessments are to be scientific in nature, it is unclear why agencies might not candidly comment on an IRIS assessment even if their comments would become part of the public record. In fact, officials from DOD, DOE, and NASA told us they did not object to EPA's plan to make interagency comments part of the public record because they would be scientific in nature and not part of a policy discussion.

While OMB officials would not comment directly on this issue as it relates to objections they might have to EPA's draft proposed process, one official told us that generally OMB believes that effective deliberations among federal agencies are important and that if agencies' deliberative comments are part of the public record, agency officials will not be as frank and candid as they would be under the protection of confidentiality.

However, transparency in the IRIS assessment process can provide assurance that these scientific assessments are appropriately based on the best available science and that they are not impacted by policy issues and considerations. Under the National Academies' risk assessment and risk management paradigm, policy considerations are relevant in the risk management phase, which occurs after the risk assessment phase that encompasses IRIS assessments.[43] Some of the federal agencies that would be given formal roles in some IRIS assessment decisions are particularly interested in risk management issues as they would likely face adverse consequences, such as increased cleanup costs and other legal liabilities, if EPA issues an IRIS assessment for a given chemical that results in a risk management decision to regulate the chemical to protect the public.[44] Consequently, to ensure credibility of the IRIS assessments, the input of these agencies into the assessment process should be transparent.

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[43] The National Academies recently addressed this issue as follows: "The committee believes that risk assessors and risk managers should talk with each other; that is, a 'conceptual distinction' does not mean establishing a wall between risk assessors and risk managers. Indeed they should have constant interaction. However, the dialogue should not bias or otherwise color the risk assessment conducted, and the activities should remain distinct; that is, risk assessors should not be performing risk management activities." National Academies, *Scientific Review of the Proposed Risk Assessment Bulletin from the Office of Management and Budget Committee to Review the OMB Risk Assessment Bulletin* (2007).

Further, when EPA and other agencies propose regulations or other actions on the basis of health risk assessments, the proposals represent policy choices. Through the rule-making process and other interagency working groups, federal agencies have the opportunity to participate in policy dialogues. Such discussions can appropriately address risk management concerns that, by definition, involve integrating risk characterization information (based, in part, on information in IRIS) with other information[45] to decide how to protect public health. In contrast, the input of federal agencies into the IRIS assessments, part of the risk assessment process, should be based solely on science issues, not policy concerns.

Conclusions

The IRIS database, one of the most significant tools that EPA has developed to effectively support its efforts to protect people and the environment from harmful chemical exposures, is at serious risk of becoming obsolete because the agency has not been able to keep its existing assessments current or complete assessments of the most important chemicals of concern. Although EPA has taken important steps to improve the IRIS program and productivity since 2000 and has developed a number of draft assessments for external review, its efforts to finalize the assessments have been thwarted by a combination of factors: the imposition of external requirements, the growing complexity and scope of risk assessments, and certain EPA management decisions. Each of these factors has led to delays in the completion of individual IRIS assessments. In addition, an overarching factor—the compounding effect of delays—has had a particularly profound impact on productivity: Even a single delay can create a cascading series of delays with far-reaching, time-consuming consequences. In fact, in some cases, it is necessary to essentially start the assessment process over because of the need to incorporate science and methodologies that have evolved since the assessments began. To effectively meet its diverse user needs, EPA must both keep the IRIS database up to date and undertake assessments of potentially dangerous chemicals not yet evaluated. Achieving these objectives will require EPA to complete IRIS assessments in a timely fashion that minimizes rework—an outcome that cannot occur unless EPA's IRIS assessment process is streamlined to routinely support timely completion of assessments. When assessments take longer than two years, they can become subject to substantial delays stemming from the need to redo key analyses to take into account changing science and assessment methodologies.

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[44] The National Academies recently emphasized that "stakeholders from all points on the spectrum of interested parties—other state and federal agencies, advocacy groups from industry, and affected communities—can be expected to offer perspectives on the risk assessment policies under discussion." National Academies, *Scientific Review of the Proposed Risk Assessment Bulletin.*

[45] "Other information" includes economic information on the costs and benefits of mitigating the risk, technological information on the feasibility of managing the risk, and the concerns of various stakeholders.

However, the manner in which other federal agencies are involved in the IRIS assessment process prevents EPA from effectively streamlining and managing its assessments. Under the current process, EPA is required to send draft assessments to OMB at two key points in the assessment process. Although the OMB/interagency reviews have no time frames or deadlines, EPA is not allowed to proceed with the assessment process until OMB agrees that EPA has sufficiently responded to agencies' comments; and OMB has also directed EPA to terminate five assessments. Further, OMB's view that disagreements between EPA and other agencies should simply be elevated to senior EPA executives for resolution is inefficient and causes delays. That is, an effective IRIS assessment process would not require the constant intervention of top-level executives, whose time is already at a premium. Moreover, the current process elevates the goal of reaching interagency agreement above achievement of IRIS program objectives and, in doing so, fails to adequately acknowledge the expertise of EPA scientists and the many other scientific experts who have prepared and reviewed the assessments. We believe that interagency coordination can enhance the quality of EPA's IRIS assessments. However, this goal would more likely be achieved if the input from other federal agencies was obtained in a manner that better ensured that EPA's scientific analyses were given appropriate weight and that provided time frames to avoid indefinite delays. Because an integral part of EPA's mission is to assess the risks associated with exposures to chemicals, the agency is best situated to establish how—and at what level—to best resolve IRIS assessment issues raised by other federal agencies. Until EPA can establish time frames for various assessment steps—including the OMB/interagency review process—and determine (1) how it will resolve interagency conflicts, (2) when assessments are ready for either independent peer review or completion, and (3) the scope of the assessments needed to support EPA programs, EPA will continue to be hampered in its ability to develop timely and credible IRIS assessments that meet its needs and protect the environment.

Importantly, the lack of transparency of the OMB/interagency review process reduces the credibility of EPA's IRIS assessments. Because the agencies' comments and the changes EPA makes in response are treated as internal executive branch documents not subject to release outside the executive branch, the OMB/interagency reviews occur in what amounts to a black box. Specifically, the first assessment drafts that become publicly available—those provided to independent peer reviews—incorporate changes from federal agencies that may be affected by the assessments without identifying or providing reasons for the changes. Moreover, the changes EPA is proposing to its current assessment process would provide potentially affected federal agencies with a formalized opportunity to provide input at almost every step in the assessment process without addressing the extent to which agencies' input would be made part of the public record. Given the importance and sensitivity of IRIS assessments, it is critical that input from all parties, particularly agencies that may be affected by the outcome, be publicly available to alleviate concerns of potential bias in the assessments.

In addition, EPA's draft proposed changes to its IRIS assessment process—which would further expand the role of other federal agencies in the process, including the option to suspend assessments of key chemicals for up to 18 months to develop new studies—would add to the already unacceptable level of delays in completing IRIS assessments. Under its draft proposed changes, EPA estimates that assessments of certain key chemicals may take up to 6 years. Assessments of this duration are problematic—they tend to get caught in a perpetual cycle of updates and revisions. Further, we believe EPA's time estimate for assessments under its draft proposal are optimistic, as most IRIS assessments currently in progress have already been in the works for more than 5 years, including 12 that have been in progress for more than 9 years. Yet these assessments have not been subject to the additional steps and requirements under the draft proposed process.

An alternative, more efficient approach to suspending assessments while waiting for new research would be for EPA to give agencies and the public more advance notice of planned assessments, thereby providing external parties with an interest in conducting additional research on a given chemical the ability to complete their work prior to the start of the IRIS assessment. This is important because effectively maintaining the IRIS database depends on strict adherence to time frames using the best available science. In addition, we note that OMB has raised questions about whether the proposed process sufficiently addresses the needs of private entities. Along these lines, we believe that if EPA grants special rights to other federal agencies to suspend IRIS assessments to conduct new research, it is likely that the agency would face pressure to do so for numerous other entities, including industries and individual companies that could be impacted by IRIS assessments should the assessments lead to regulatory actions.

Further, while we believe it is appropriate for EPA to identify key uncertainties in IRIS assessments and to continue to work on developing methodologies for conducting more sophisticated and meaningful uncertainty analyses, continuing to delay IRIS assessments in order to develop and test enhanced methodologies and strategies for communicating them can conflict with EPA's stated goal of seeking balance among fairness, accuracy, and efficient action. More specifically, EPA has acknowledged that not acting until data quality improves can result in substantial harm to human health, safety, and the environment. Also, as EPA continues to incorporate uncertainty analysis in its assessments, ensuring that the information is clear and useful to decision makers is important. Along these lines, the National Academies and others have warned that producing "ranges of meaningless and confusing risk estimates" could result in assessments of reduced, rather than enhanced, quality and objectivity.

Lastly, while it is difficult to overstate the importance of the IRIS program to EPA's ability to effectively conduct its mission of protecting human health and the environment, this program currently uses about 0.1 percent of EPA's annual appropriations—specifically, in fiscal year 2007, the program received about $9.6 million of EPA's $7.3 billion budget. EPA's current estimate that it will be able to complete 16 assessments a year by 2011 would represent a substantial increase over recent productivity; however, it is not clear that this level will be sufficient to maintain the viability of the IRIS database.

Recommendations for Executive Action

To develop timely chemical risk information that EPA needs to effectively conduct its mission, we are recommending that the Administrator, EPA, require the Office of Research and Development to re-evaluate its draft proposed changes to the IRIS assessment process in light of the issues raised in this report and ensure that any revised process

- clearly defines and documents a streamlined IRIS assessment process that can be conducted within time frames that minimize the need for wasteful rework and carefully considers the trade-off between the benefits of changes that involve additional steps and time—including the development of enhanced uncertainty analyses and other emerging assessment methods—and the impacts of these changes on EPA's ability to complete timely chemical assessments;
- establishes a policy that endorses conducting IRIS assessments on the basis of peer-reviewed scientific studies available at the time of the assessment and develops criteria for allowing assessments to be suspended to await the completion of scientific studies only under exceptional circumstances;
- establishes IRIS assessment needs to provide at least 2 years' notice of assessments that are planned, including criteria for making exceptions to the advance notifications, if needed;
- sets time limits for all parties, including OMB and other federal agencies, to provide comments to EPA on draft IRIS assessments; and
- periodically assesses the level of resources that should be dedicated to this significant program to meet user needs and maintain a viable IRIS database.

In addition, we recommend that the EPA Administrator take steps to better ensure that EPA has the ability to develop transparent, credible IRIS chemical assessments—an ability that relies in large part on EPA's independence in conducting these important assessments. Actions that are key to this ability include ensuring that EPA

- can determine the types of IRIS assessments to conduct on the basis of the needs of EPA's program offices and other users;
- can define the appropriate role of external federal agencies in EPA's IRIS assessment process and manage an interagency review process in a manner that enhances the quality, transparency, timeliness, and credibility of IRIS assessments, including determining when interagency issues have been appropriately addressed; and
- has the ability to provide comments by OMB and other federal agencies on draft IRIS assessments to decision makers, the Congress, and the public.

Agency Comments and Our Evaluation

In commenting on a draft of this report, EPA's Assistant Administrator for Research and Development agreed to consider our recommendations in revising the IRIS assessment process. However, EPA stated that it believed the productivity and transparency issues discussed in the draft report were misrepresented in the title and body of the report. We disagree and believe we have fairly represented IRIS productivity and transparency issues related to the IRIS assessment process. We did clarify that the transparency issues highlighted in our report focus on the IRIS assessment process rather than on the content of IRIS assessments, and we revised the report title. In addition, EPA emphasized that the proposed changes to the IRIS assessment process are still subject to change. Along these lines, we made our recommendations with the intent that they would be integrated into any revised process. In its response, EPA also estimated that under the new process, most assessments would take between 3 and 4-1/2 years; mission-critical assessments would take up to 6 years. These estimates differ from the time frames EPA officials provided during our review, and we have revised the report to reflect this. However, we believe an IRIS assessment process built around such time frames is problematic. As we state in our draft and final reports, when assessments take longer than 2 years, they can become subject to substantial delays stemming from the need to redo key analyses to take into account changing science and assessment methodologies. Finally, EPA asserted that the new process will lead to increased productivity. We disagree and have concluded that the proposed revisions would add to the already unacceptable level of delays in completing IRIS assessments.

In its comments, OMB did not specifically address the recommendations we made to EPA but disagreed with some aspects of the report, primarily regarding our characterization of the OMB-managed interagency reviews and their effects on IRIS assessments. For example, OMB indicated that it disagreed with our conclusions that the OMB/interagency reviews make it more difficult for EPA to complete IRIS assessments in a timely manner, that these reviews affect the credibility of the assessments, and that interagency comments should be transparent. We disagree with OMB and believe that we have fairly represented the OMB/interagency review process as well as the importance of input from all parties being publicly available. Given the importance and sensitivity of IRIS assessments, it is critical that input from all parties, particularly agencies that may be affected by the outcome, be publicly available to alleviate concerns of potential bias in the assessments. EPA's and OMB's comments and our detailed responses appear in appendix IV and appendix V.

As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution of this report until 30 days from the report date. At that time, we will send copies to the Administrator, EPA; the Director, OMB; and appropriate congressional committees and other interested parties. We will also make copies available to others on request. In addition, the report will be available at no charge on the GAO Web site at http://www.gao.gov.

If you or your staff have any questions about this report, please contact me at (202) 512-3841 or stephensonj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix VI.

Sincerely yours,

John B. Stephenson
Director, Natural Resources
and Environment

Appendix I: Objectives, Scope, and Methodology

This appendix details the methods we used to assess the Environmental Protection Agency's (EPA) management of its Integrated Risk Information System (IRIS). For this review, we determined (1) the outcome of steps that EPA has taken to ensure that IRIS contains current, credible chemical risk information, to address the backlog of IRIS assessments, and to respond to new requirements from the Office of Management and Budget (OMB); and (2) the potential effects of EPA's planned changes to the IRIS assessment process on EPA's ability to ensure that IRIS provides current, credible risk information.

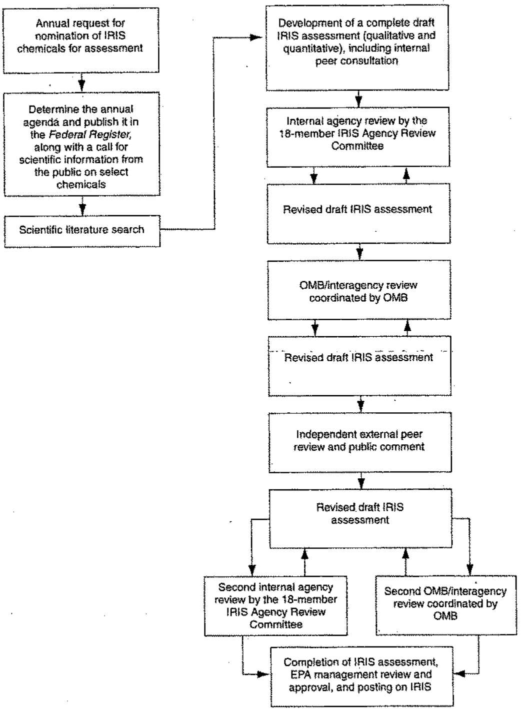
To address these two objectives, we reviewed relevant EPA and other documents, including EPA's 2003 IRIS Needs Assessment, the Office of Research and Development's multiyear plans, numerous documents outlining the IRIS assessment process and draft proposed changes to the assessment process, EPA budget justification documents, and OMB's Program Assessment Rating Tool assessment that covered the IRIS program. We interviewed officials from EPA's National Center for Environmental Assessment who manage the IRIS assessment program, including the Center Director, the Associate Director for Health, and the IRIS Program Director; officials from other EPA program offices, including the Office of Air and Radiation; and officials from federal science and health agencies that are involved in the IRIS assessment process, to obtain their perspectives on, among other things, the current IRIS assessment process, the potential effects of the draft proposed changes to the process, the extent to which EPA has made progress in completing assessments and meeting user needs, and challenges EPA faces in completing assessments. In addition, we interviewed officials from the Department of Defense, the Department of Energy, and the National Aeronautics and Space Administration who have served on the interagency working group on the IRIS assessment process, and OMB officials in the Office of General Counsel and the Office of Information and Regulatory Affairs to obtain their perspectives on the OMB/interagency review process and on the planned changes to the IRIS assessment process. We also interviewed officials from the Department of Health and Human Services' Agency for Toxic Substances and Disease Registry (ATSDR), an agency that assesses the potential noncancer health effects of exposure to some chemicals, to obtain information on ATSDR's assessment process. In addition, we attended the Board of Scientific Counselors Human Health Risk Assessment (HHRA) Subcommittee meetings in November 2007. During these meetings, the Subcommittee reviewed the EPA Office of Research and Development's HHRA program—specifically, its relevance, quality, performance, and scientific leadership.

For the first objective, we obtained and analyzed several data sets, including data from EPA's IRIS database; EPA's IRIS Track—a compilation of status reports for IRIS assessments in progress; *Federal Register* notices announcing annual IRIS agendas; a spreadsheet that EPA uses to track the IRIS assessments sent to OMB for the OMB/interagency reviews; EPA's 2003 screening level reviews report—its efforts to identify assessments that may need to be updated; and EPA's 2003 IRIS Needs Assessment. From the data we gathered, we analyzed information on EPA's productivity, including the number of new and completed IRIS assessments, for fiscal years 2000 through 2007; the status of IRIS assessments, as of December 1, 2007, that were in progress during fiscal year 2007; the status of IRIS assessments that have been sent to OMB for OMB/interagency review and the time elapsed during those reviews; the number of assessments in the IRIS database that may need to be updated; the resources provided to the program for fiscal years 2000 through 2007; and user needs and EPA's assessment completion goals. We also interviewed chemical managers, who are responsible for managing the IRIS assessments in progress, to obtain further information on the 77 chemicals in progress during fiscal year 2007. We did not evaluate the scientific content or quality of IRIS assessments.

In addition, we conducted a reliability review of the data we received from EPA for our first objective. Through our review, we determined that the data we used were sufficiently reliable for our purposes. Our assessment consisted of interviews with officials about the data system and elements and the method of data input, among other areas. We also corroborated the data with other sources, where possible. For example, we verified the information provided in EPA's IRIS Track system with the chemical managers responsible for each of the 77 chemicals in progress during fiscal year 2007, and updated the information as appropriate. Similarly, we ensured that status information presented in IRIS Track was consistent with the status information presented in the spreadsheet that EPA uses to track draft assessments provided to OMB for the OMB/interagency review. In addition, EPA attempted to corroborate its data on the status of IRIS assessments that have been sent to OMB for OMB/interagency review and the time elapsed during those reviews, providing OMB with its tracking spreadsheet for review. OMB chose not to respond. Consequently, we relied on EPA's data and assessed its reliability, based on information including the source of the data and method of input.

We conducted this performance audit from October 2006 to March 2008 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix II: Broad Outline of EPA's Current IRIS Assessment Process


Annual request for nomination of IRIS chemicals for assessment
Determine the annual agenda and publish it in the *Federal Register*, along with a call for scientific information from the public on select chemicals
Scientific literature search
Development of a complete draft IRIS assessment (qualitative and quantitative), including internal peer consultation
Internal agency review by the 18-member IRIS Agency Review Committee
Revised draft IRIS assessment
OMB/interagency review coordinated by OMB
Revised draft IRIS assessment
Independent external peer review and public comment
Revised draft IRIS assessment
Second internal agency review by the 18-member IRIS Agency Review Committee
Second OMB/interagency review coordinated by OMB
Completion of IRIS assessment, EPA management review and approval, and posting on IRIS

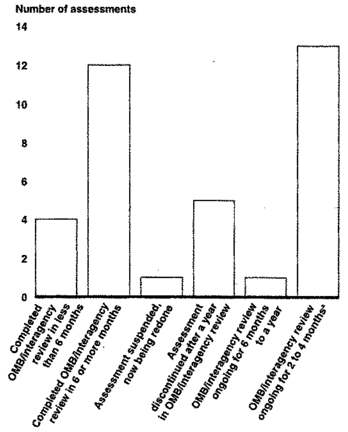
Source: GAO analysis of EPA information.

Note: This outline does not include the individual activities, including internal reviews and briefings, encompassed within many of the broad IRIS assessment categories.

Appendix III: Information on OMB/Interagency Reviews of IRIS Assessments

As of December 1, 2007, EPA has sent 36 draft IRIS assessments to OMB for the first OMB/interagency review managed by OMB, and the reviews of 16 assessments were completed. As shown in figure 6, the OMB/interagency review of 4 assessments was completed in less than 6 months and 12 of these assessments added 6 or more months to the IRIS assessment process.

Figure 6: Status of IRIS Assessments Sent to OMB for the First OMB/Interagency Review Starting in Fiscal Year 2004, as of December 1, 2007



Source: GAO analysis of EPA data.

[a] These 13 assessments were submitted to OMB in the last quarter of fiscal year 2007.

Moreover, as also shown in figure 6, five assessments that assessed acute exposure were discontinued at the direction of OMB after a year in the

OMB/interagency review stage,[1] and one assessment was suspended and is now being redone (naphthalene). Finally, 14 assessments were at the OMB/interagency review stage as of December 1, 2007: Of these, 1 had been at this stage for 9-½ months, and the remaining 13 had been submitted to OMB in the last quarter of fiscal year 2007 and had been at the OMB/interagency review stage for 2 to 4 months. While OMB officials said that EPA does not have to provide a document addressing every OMB/interagency comment, EPA officials said that a detailed disposition of comments document was, in fact, necessary in order to get OMB's agreement that EPA had satisfactorily addressed all comments. There are no time frames for this iterative process.

OMB officials said that the second OMB/interagency review is conducted by OMB to ensure that EPA has adequately considered the comments from the external peer review panel. As of December 1, 2007, 10 assessments had been sent to OMB for the second OMB/interagency review, and 5 of these assessments completed the review. The time frames for these five assessments ranged from 10 days to almost 4 months.

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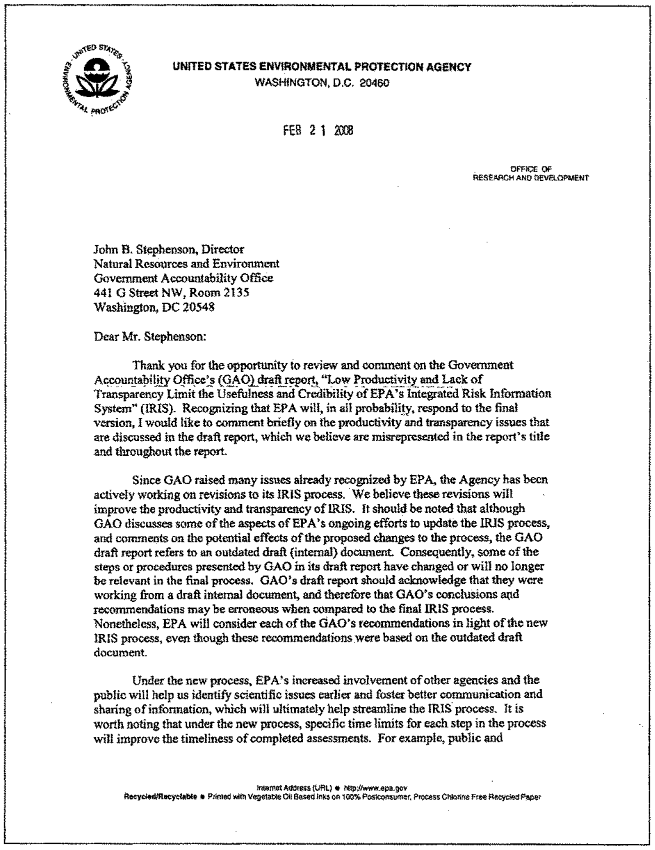
[1] These five assessments address short-term health risks. According to EPA, while OMB had previously agreed that these assessments would be included in EPA's 2006 annual performance goals that OMB uses to evaluate EPA's performance, in November 2007, OMB told EPA that it would not count EPA's short-term assessments toward meeting its goals, thereby lowering EPA's performance rating by OMB.

Appendix IV: Comments from the Environmental Protection Agency

Note: GAO comments supplementing those in the report text appear at the end of this appendix.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 2 1 2008

OFFICE OF
RESEARCH AND DEVELOPMENT

John B. Stephenson, Director
Natural Resources and Environment
Government Accountability Office
441 G Street NW, Room 2135
Washington, DC 20548

Dear Mr. Stephenson:

Thank you for the opportunity to review and comment on the Government Accountability Office's (GAO) draft report, "Low Productivity and Lack of Transparency Limit the Usefulness and Credibility of EPA's Integrated Risk Information System" (IRIS). Recognizing that EPA will, in all probability, respond to the final version, I would like to comment briefly on the productivity and transparency issues that are discussed in the draft report, which we believe are misrepresented in the report's title and throughout the report.

Since GAO raised many issues already recognized by EPA, the Agency has been actively working on revisions to its IRIS process. We believe these revisions will improve the productivity and transparency of IRIS. It should be noted that although GAO discusses some of the aspects of EPA's ongoing efforts to update the IRIS process, and comments on the potential effects of the proposed changes to the process, the GAO draft report refers to an outdated draft (internal) document. Consequently, some of the steps or procedures presented by GAO in its draft report have changed or will no longer be relevant in the final process. GAO's draft report should acknowledge that they were working from a draft internal document, and therefore that GAO's conclusions and recommendations may be erroneous when compared to the final IRIS process. Nonetheless, EPA will consider each of the GAO's recommendations in light of the new IRIS process, even though these recommendations were based on the outdated draft document.

See comment 1.

See comment 2.

Under the new process, EPA's increased involvement of other agencies and the public will help us identify scientific issues earlier and foster better communication and sharing of information, which will ultimately help streamline the IRIS process. It is worth noting that under the new process, specific time limits for each step in the process will improve the timeliness of completed assessments. For example, public and

See comment 3.

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See comment 4.

interagency review periods will be for fixed and relatively short durations. Interagency and public review will therefore represent only a small fraction of the total time required to complete an IRIS assessment. For most chemicals, the IRIS process will take between three and four and a half years. For the small number of mission-critical chemicals, the process may take an extra one to one and a half years. EPA believes the new IRIS process, in combination with the increased resources for the program provided in recent years, will lead to increased productivity in achieving completed assessments.

See comment 5.

See comment 6.

Although only briefly recognized in GAO's draft report, today's IRIS assessments are much more sophisticated, complex, and of higher scientific quality than at any other time in the program's history. The increased complexity of chemical assessments often leads to extensive public comments and more rigorous levels of internal and external peer review, which is one of the most important reasons for delays in the IRIS process. Additionally, recent external peer reviews by EPA's Science Advisory Board (SAB) and the National Academy of Sciences (NAS) have requested that even more sophisticated analyses, such as quantitative uncertainty analysis, be performed and presented in some IRIS assessments. These issues, and EPA's responsiveness to them, are given too little attention or are unfairly criticized in the GAO draft report.

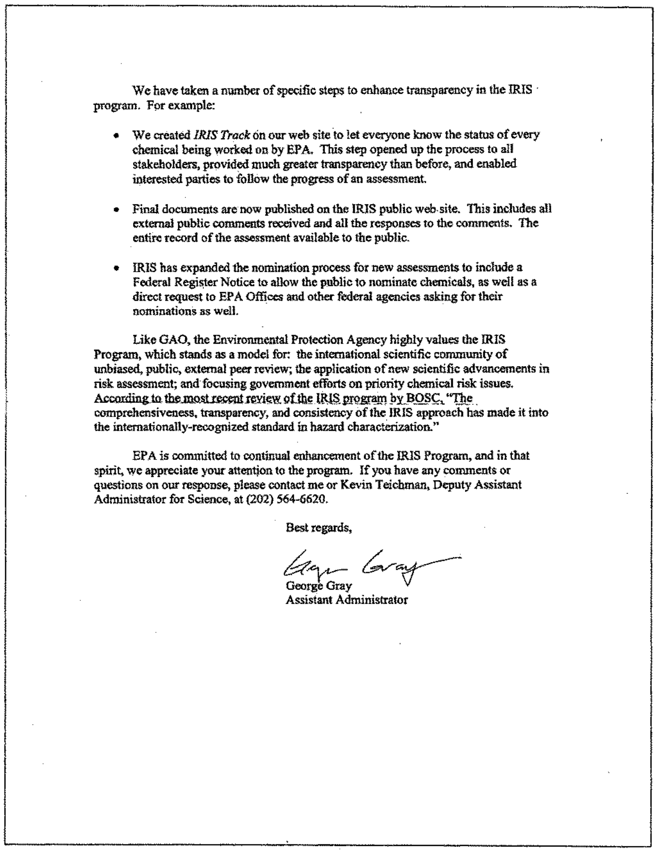
See comment 7.

Also, the IRIS program has increased the rigor of its scientific peer review. Specifically, the external peer review process has been changed from letter reviews to face-to-face panel peer reviews that are open to the public. This has encouraged public interaction with the peer reviewers. Members of our Board of Scientific Counselors (BOSC) that recently reviewed the IRIS program indicated that "the extent of peer review for IRIS . . . exceeds most other examples with which the subcommittee members were familiar."

See comment 8.

See comment 9.

Transparency is critical to an effective IRIS process. It is equally important that scientists and policymakers be able to have full and frank discussions. Clearly, the quality of government decisions is better and stronger when healthy skepticism is not discouraged. The current IRIS process strikes a balance between these two principles by encouraging open discussion of science and science policy questions, while appropriately protecting the deliberative process. Enhancing transparency through these and other measures necessarily means bringing many parties into the IRIS process. However, increased participation does not diminish EPA's accountability as the final decision-maker in establishing IRIS health values. All final IRIS assessments must also stand on their own merit by undergoing public and external peer review. It is noteworthy that in addition to having a transparent process, it is important to ensure transparency in the content of IRIS assessments (e.g., the rationale for relying on or using specific data sets, assumptions, or models). The GAO draft report does not comment on this facet of transparency, which directly bears on the content and quality of IRIS assessments.



We have taken a number of specific steps to enhance transparency in the IRIS program. For example:

See comment 10.

- We created *IRIS Track* on our web site to let everyone know the status of every chemical being worked on by EPA. This step opened up the process to all stakeholders, provided much greater transparency than before, and enabled interested parties to follow the progress of an assessment.

See comment 11.

- Final documents are now published on the IRIS public web site. This includes all external public comments received and all the responses to the comments. The entire record of the assessment available to the public.

See comment 12.

- IRIS has expanded the nomination process for new assessments to include a Federal Register Notice to allow the public to nominate chemicals, as well as a direct request to EPA Offices and other federal agencies asking for their nominations as well.

Like GAO, the Environmental Protection Agency highly values the IRIS Program, which stands as a model for: the international scientific community of unbiased, public, external peer review; the application of new scientific advancements in risk assessment; and focusing government efforts on priority chemical risk issues. According to the most recent review of the IRIS program by BOSC, "The comprehensiveness, transparency, and consistency of the IRIS approach has made it into the internationally-recognized standard in hazard characterization."

EPA is committed to continual enhancement of the IRIS Program, and in that spirit, we appreciate your attention to the program. If you have any comments or questions on our response, please contact me or Kevin Teichman, Deputy Assistant Administrator for Science, at (202) 564-6620.

Best regards,

George Gray

George Gray
Assistant Administrator

The following are GAO's comments on the Environmental Protection Agency's letter dated February 21, 2008.

GAO Comments

1. Our analysis of the draft proposed changes to the IRIS assessment process does not support EPA's assertion that the revised process EPA is developing will improve the productivity and transparency of IRIS. In fact, as discussed in our draft and final reports, the draft proposed process would exacerbate existing productivity and transparency concerns.

2. EPA emphasizes that our draft report includes information on proposed revisions to the IRIS assessment process that "have changed or will no longer be relevant" in the final version. Our draft and final reports clearly indicate that we are providing information on EPA's current assessment process as well as on proposed changes to the IRIS process that EPA has been developing for years—but has not yet finalized. For example, the draft and final reports state that "as of December 2007, EPA was planning to send a revised draft back to the interagency work group for review and approval." Moreover, in the draft and final reports, the graphic outlining the proposed changes is titled "EPA's Draft Proposed IRIS Assessment Process." Further, we made our recommendations with the intent that they be considered and integrated into any revised process that EPA finalizes. Finally, we note that EPA did not identify any significant changes it has made to the proposed process we outline in the draft and final reports, either when it commented on the draft report or on a December 2007 statement of facts provided to EPA for review for factual accuracy. However, to ensure clarity, we have added "draft" prior to our use of the term "proposed process" in a number of places.

3. EPA states that "under the new process," the increased early involvement of other agencies and the public in identifying scientific issues and sharing information will ultimately help streamline the IRIS process. We note that other agencies and the public have the opportunity for early involvement in IRIS assessments under the current process. We do not believe that simply formalizing their involvement will, in fact, streamline the process or improve the timeliness of completed assessments.

4. We have revised the report to add the updated estimated time frames for IRIS assessments under EPA's proposed revisions to the process provided in EPA's letter. With most assessments estimated to take up to 4-1/2 years to complete, it appears unlikely that the IRIS program

will be able to produce quality assessments in a timely manner. As discussed in our draft and final reports, when assessments take longer than 2 years, they can become subject to substantial delays stemming from the need to redo key analyses to take into account changing science and assessment methodologies. Further, although EPA states that only a small number of IRIS assessments will be designated as mission-critical, we note that the chemicals with this designation are likely to be those posing widespread public health concerns that need to be addressed expeditiously. As we state in the draft and final reports, effectively maintaining the IRIS database will depend on strict adherence to time frames using the best available science.

In addition, we believe that if EPA grants special rights to other federal agencies to, among other things, suspend IRIS assessments to conduct new research, it is likely that the agency would face pressure to do so for other entities, including industries and individual companies that could be impacted by IRIS assessments should they lead to regulatory actions. Therefore, while EPA's stated intent is to limit the number of mission-critical designations made by other federal agencies, the number is likely to increase over time.

5. While EPA states that the draft report only briefly recognizes that IRIS assessments are more sophisticated and complex, our draft and final reports identify the growing complexity of risk assessments and risk assessment methods and models as one of five key factors contributing to EPA's inability to complete IRIS assessments in a timely manner.

6. EPA states that external peer reviews have requested that more sophisticated analyses, such as quantitative uncertainty analysis, be performed and presented in some IRIS assessments. EPA further states that its responsiveness to these requests is given too little attention or is unfairly criticized in the draft report. In fact, our draft and final reports clearly state that peer reviews of EPA's assessments have sometimes recommended additional uncertainty analysis. Further, while we conclude that it is appropriate for EPA to identify key uncertainties in IRIS assessments and to continue to work on developing methodologies for conducting more sophisticated and meaningful uncertainty analyses, the methodologies are not yet developed. That is, our draft and final reports indicate that EPA plans to release draft reports in 2010 on methods for analyzing and characterizing uncertainty in hazard and dose response and in physiologically based pharmacokinetic models. Thus, we believe that continuing to delay IRIS assessments to develop and test enhanced

methodologies and strategies for communicating them conflicts with EPA's stated goal of seeking balance among fairness, accuracy, and efficient action. Specifically, it is unclear how EPA's ongoing, nearly 2-year delay of the assessment of tetrachloroethylene (perc)—a widespread groundwater contaminant—pending the development of an acceptable uncertainty analysis represents an appropriate balance between accuracy and efficient action.

7. The draft and final reports discuss the changes EPA has made to its IRIS assessment process, including the one highlighted in EPA's letter—a change from letter peer reviews to panel peer reviews open to the public.

8. EPA states that the current IRIS process strikes a balance between transparency and having full and frank discussions by encouraging open discussion of science and science policy questions while appropriately protecting the deliberative process. We disagree that such a balance exists because the OMB/interagency review process is not transparent at all. In its comments, EPA dismisses any impact of the opaque OMB/interagency review process, emphasizing that all IRIS assessments undergo public and external peer review. However, the presence of transparency at a later stage of IRIS assessment development does not excuse or explain its absence earlier. Further, the National Academies have stated that the dialogue between risk assessors and risk managers should not bias or otherwise color the risk assessment conducted, and risk assessment and risk management activities should remain distinct. Transparency in the IRIS assessment process can provide assurance that these scientific assessments are appropriately based on the best available science and that they are not impacted by policy issues and considerations. Finally, because federal agencies' comments on IRIS assessments provided via the OMB/interagency process are to be scientific in nature, it is unclear why agencies would not candidly comment on an IRIS assessment even if their comments would become part of the public record.

9. EPA's comments note that transparency is applicable to both the assessment process and the content of IRIS assessments (e.g., the rationale for relying on or using specific data sets, assumptions, and models). We have revised our report to recognize that transparency is relevant to both the assessment process and the content of IRIS assessments and to be clear that the transparency issues we discuss primarily relate to the process. We note that many of the process changes EPA has made beginning in the 1990s are aimed at improving

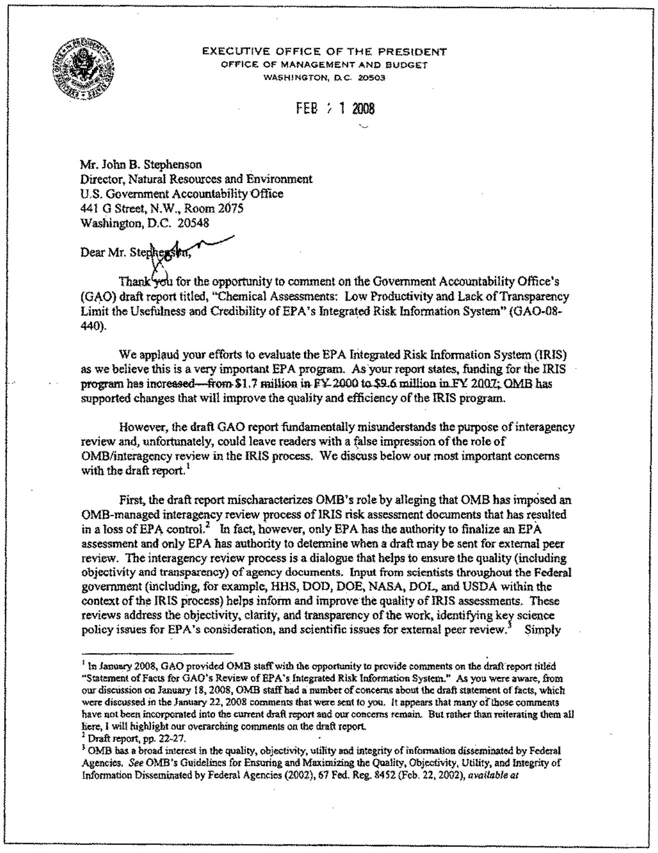
the transparency of the content of IRIS assessments as well as the process.

10. This information on EPA process improvements is provided in the draft and final reports.

11. EPA stated that final IRIS documents are now published on the IRIS public Web site and that the entire record is available to the public. This statement is not accurate because the record of the OMB/interagency review comments and EPA's responses to them are not made available to the public.

12. The draft and final reports provide information on EPA's nomination process for new assessments, which includes a *Federal Register* notice.

Appendix V: Comments from the Office of Management and Budget



EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

FEB 21 2008

Mr. John B. Stephenson
Director, Natural Resources and Environment
U.S. Government Accountability Office
441 G Street, N.W., Room 2075
Washington, D.C. 20548

Dear Mr. Stephenson,

Thank you for the opportunity to comment on the Government Accountability Office's (GAO) draft report titled, "Chemical Assessments: Low Productivity and Lack of Transparency Limit the Usefulness and Credibility of EPA's Integrated Risk Information System" (GAO-08-440).

We applaud your efforts to evaluate the EPA Integrated Risk Information System (IRIS) as we believe this is a very important EPA program. As your report states, funding for the IRIS program has increased—from $1.7 million in FY 2000 to $9.6 million in FY 2007; OMB has supported changes that will improve the quality and efficiency of the IRIS program.

However, the draft GAO report fundamentally misunderstands the purpose of interagency review and, unfortunately, could leave readers with a false impression of the role of OMB/interagency review in the IRIS process. We discuss below our most important concerns with the draft report.[1]

See comment 1.

First, the draft report mischaracterizes OMB's role by alleging that OMB has imposed an OMB-managed interagency review process of IRIS risk assessment documents that has resulted in a loss of EPA control.[2] In fact, however, only EPA has the authority to finalize an EPA assessment and only EPA has authority to determine when a draft may be sent for external peer review. The interagency review process is a dialogue that helps to ensure the quality (including objectivity and transparency) of agency documents. Input from scientists throughout the Federal government (including, for example, HHS, DOD, DOE, NASA, DOL, and USDA within the context of the IRIS process) helps inform and improve the quality of IRIS assessments. These reviews address the objectivity, clarity, and transparency of the work, identifying key science policy issues for EPA's consideration, and scientific issues for external peer review.[3] Simply

See comment 2.

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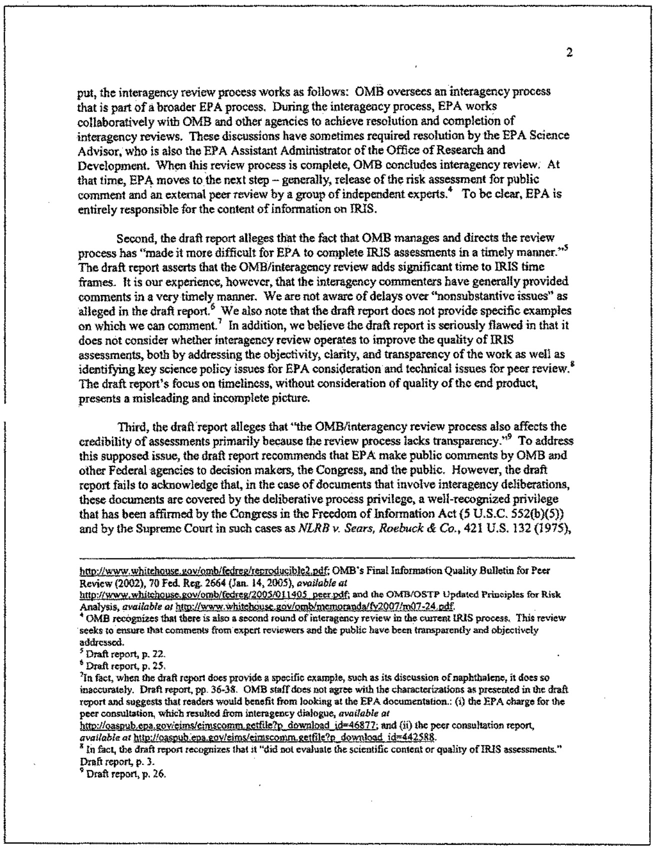
[1] In January 2008, GAO provided OMB staff with the opportunity to provide comments on the draft report titled "Statement of Facts for GAO's Review of EPA's Integrated Risk Information System." As you were aware, from our discussion on January 18, 2008, OMB staff had a number of concerns about the draft statement of facts, which were discussed in the January 22, 2008 comments that were sent to you. It appears that many of those comments have not been incorporated into the current draft report and our concerns remain. But rather than reiterating them all here, I will highlight our overarching comments on the draft report.

[2] Draft report, pp. 22-27.

[3] OMB has a broad interest in the quality, objectivity, utility and integrity of information disseminated by Federal Agencies. *See* OMB's Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies (2002), 67 Fed. Reg. 8452 (Feb. 22, 2002), *available at*



put, the interagency review process works as follows: OMB oversees an interagency process that is part of a broader EPA process. During the interagency process, EPA works collaboratively with OMB and other agencies to achieve resolution and completion of interagency reviews. These discussions have sometimes required resolution by the EPA Science Advisor, who is also the EPA Assistant Administrator of the Office of Research and Development. When this review process is complete, OMB concludes interagency review. At that time, EPA moves to the next step – generally, release of the risk assessment for public comment and an external peer review by a group of independent experts.[4] To be clear, EPA is entirely responsible for the content of information on IRIS.

See comment 3.

See comment 4.

Second, the draft report alleges that the fact that OMB manages and directs the review process has "made it more difficult for EPA to complete IRIS assessments in a timely manner."[5] The draft report asserts that the OMB/interagency review adds significant time to IRIS time frames. It is our experience, however, that the interagency commenters have generally provided comments in a very timely manner. We are not aware of delays over "nonsubstantive issues" as alleged in the draft report.[6] We also note that the draft report does not provide specific examples on which we can comment.[7] In addition, we believe the draft report is seriously flawed in that it does not consider whether interagency review operates to improve the quality of IRIS assessments, both by addressing the objectivity, clarity, and transparency of the work as well as identifying key science policy issues for EPA consideration and technical issues for peer review.[8] The draft report's focus on timeliness, without consideration of quality of the end product, presents a misleading and incomplete picture.

See comment 5.

Third, the draft report alleges that "the OMB/interagency review process also affects the credibility of assessments primarily because the review process lacks transparency."[9] To address this supposed issue, the draft report recommends that EPA make public comments by OMB and other Federal agencies to decision makers, the Congress, and the public. However, the draft report fails to acknowledge that, in the case of documents that involve interagency deliberations, these documents are covered by the deliberative process privilege, a well-recognized privilege that has been affirmed by the Congress in the Freedom of Information Act (5 U.S.C. 552(b)(5)) and by the Supreme Court in such cases as *NLRB v. Sears, Roebuck & Co.*, 421 U.S. 132 (1975),

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http://www.whitehouse.gov/omb/fedreg/reproducible2.pdf; OMB's Final Information Quality Bulletin for Peer Review (2002), 70 Fed. Reg. 2664 (Jan. 14, 2005), *available at* http://www.whitehouse.gov/omb/fedreg/2005/011405_peer.pdf; and the OMB/OSTP Updated Principles for Risk Analysis, *available at* http://www.whitehouse.gov/omb/memoranda/fy2007/m07-24.pdf.

[4] OMB recognizes that there is also a second round of interagency review in the current IRIS process. This review seeks to ensure that comments from expert reviewers and the public have been transparently and objectively addressed.

[5] Draft report, p. 22.

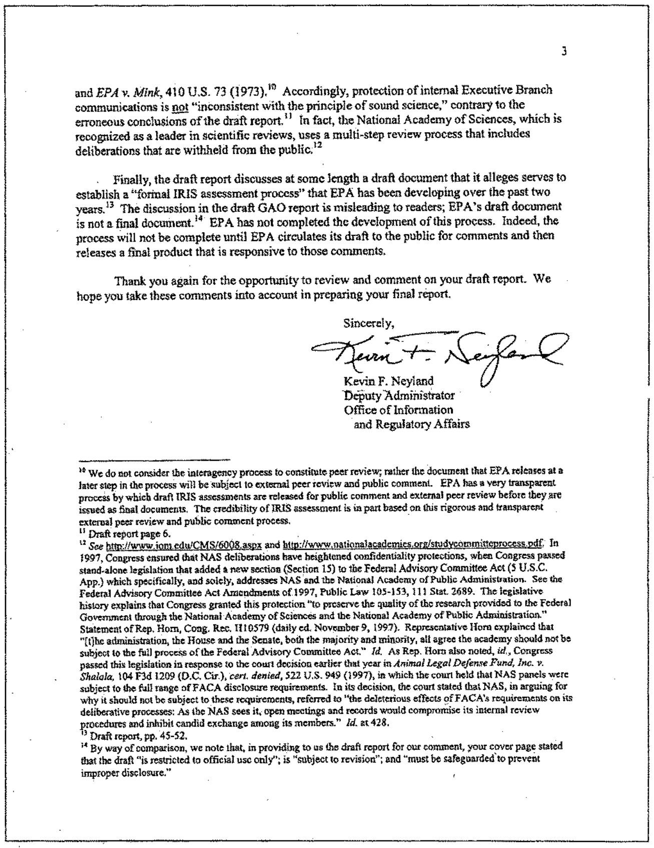
[6] Draft report, p. 25.

See comment 6.

[7] In fact, when the draft report does provide a specific example, such as its discussion of naphthalene, it does so inaccurately. Draft report, pp. 36-38. OMB staff does not agree with the characterizations as presented in the draft report and suggests that readers would benefit from looking at the EPA documentation.: (i) the EPA charge for the peer consultation, which resulted from interagency dialogue, *available at* http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=46877; and (ii) the peer consultation report, *available at* http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=442588.

[8] In fact, the draft report recognizes that it "did not evaluate the scientific content or quality of IRIS assessments." Draft report, p. 3.

[9] Draft report, p. 26.



3

and *EPA v. Mink*, 410 U.S. 73 (1973).[10] Accordingly, protection of internal Executive Branch communications is not "inconsistent with the principle of sound science," contrary to the erroneous conclusions of the draft report.[11] In fact, the National Academy of Sciences, which is recognized as a leader in scientific reviews, uses a multi-step review process that includes deliberations that are withheld from the public.[12]

See comment 7.

Finally, the draft report discusses at some length a draft document that it alleges serves to establish a "formal IRIS assessment process" that EPA has been developing over the past two years.[13] The discussion in the draft GAO report is misleading to readers; EPA's draft document is not a final document.[14] EPA has not completed the development of this process. Indeed, the process will not be complete until EPA circulates its draft to the public for comments and then releases a final product that is responsive to those comments.

Thank you again for the opportunity to review and comment on your draft report. We hope you take these comments into account in preparing your final report.

Sincerely,

Kevin F. Neyland
Deputy Administrator
Office of Information
and Regulatory Affairs

See comment 8.

[10] We do not consider the interagency process to constitute peer review; rather the document that EPA releases at a later step in the process will be subject to external peer review and public comment. EPA has a very transparent process by which draft IRIS assessments are released for public comment and external peer review before they are issued as final documents. The credibility of IRIS assessment is in part based on this rigorous and transparent external peer review and public comment process.

[11] Draft report page 6.

See comment 9.

[12] *See* http://www.iom.edu/CMS/6008.aspx and http://www.nationalacademies.org/studycommitteprocess.pdf. In 1997, Congress ensured that NAS deliberations have heightened confidentiality protections, when Congress passed stand-alone legislation that added a new section (Section 15) to the Federal Advisory Committee Act (5 U.S.C. App.) which specifically, and solely, addresses NAS and the National Academy of Public Administration. See the Federal Advisory Committee Act Amendments of 1997, Public Law 105-153, 111 Stat. 2689. The legislative history explains that Congress granted this protection "to preserve the quality of the research provided to the Federal Government through the National Academy of Sciences and the National Academy of Public Administration." Statement of Rep. Horn, Cong. Rec. H10579 (daily ed. November 9, 1997). Representative Horn explained that "[t]he administration, the House and the Senate, both the majority and minority, all agree the academy should not be subject to the full process of the Federal Advisory Committee Act." *Id.* As Rep. Horn also noted, *id.*, Congress passed this legislation in response to the court decision earlier that year in *Animal Legal Defense Fund, Inc. v. Shalala,* 104 F3d 1209 (D.C. Cir.), *cert. denied*, 522 U.S. 949 (1997), in which the court held that NAS panels were subject to the full range of FACA disclosure requirements. In its decision, the court stated that NAS, in arguing for why it should not be subject to these requirements, referred to "the deleterious effects of FACA's requirements on its deliberative processes: As the NAS sees it, open meetings and records would compromise its internal review procedures and inhibit candid exchange among its members." *Id.* at 428.

[13] Draft report, pp. 45-52.

See comment 10.

[14] By way of comparison, we note that, in providing to us the draft report for our comment, your cover page stated that the draft "is restricted to official use only"; is "subject to revision"; and "must be safeguarded to prevent improper disclosure."

The following are GAO's comments on the Office of Management and Budget's letter dated February 21, 2008.

GAO Comments

1. OMB states that the draft report mischaracterizes OMB's role by alleging that OMB has imposed an OMB-managed interagency review process of IRIS risk assessment documents that has resulted in a loss of EPA control. We believe that we have appropriately described the OMB/interagency review process and identified the time frame and assessment content limitations it has placed on EPA. First, as discussed in the draft and final reports, OMB has limited EPA's ability to determine the types of assessments it will conduct to meet its program needs by requiring EPA to terminate five IRIS assessments. Second, while EPA's annual performance goal for IRIS assessments had been the number of completed assessments, during the Program Assessment Rating Tool review by OMB it was agreed that the number of assessments provided to OMB for OMB/interagency review was the most appropriate annual measure of performance because EPA "relinquishes direct control of production dates" when it sends draft IRIS assessments to OMB. Third, our draft and final reports are clear that EPA officially determines when drafts are sent for external peer review or are finalized, but they are also clear that prior to taking these steps, EPA must be notified by OMB that EPA has adequately addressed interagency comments. Thus, the current process elevates the goal of reaching interagency agreement above achieving IRIS program objectives and in doing so fails to adequately acknowledge the expertise of EPA scientists and the many other scientific experts who have prepared and reviewed the assessments. Importantly, the fact that the first assessment drafts that become publicly available—those provided to independent peer reviewers—incorporate changes from federal agencies that may be affected by the assessments without identifying these changes or the reasons they were made weakens the credibility of the assessments. Finally, because the negotiations over OMB/interagency comments are not disclosed, OMB's assertion that EPA is entirely responsible for the content of information on IRIS is open to question.

2. GAO provides statements of facts to agencies to confirm the factual accuracy of statements upon which reports are based. OMB commented that we did not incorporate its concerns about the draft statement of facts we provided to OMB. We considered OMB's comments that addressed factual information and, in response, made some revisions as appropriate. However, many of OMB's comments did not address facts but were focused on broader issues, such as the

scope and methodology of our review. We disagreed with OMB's broad comments and thus did not make certain changes OMB suggested. For example, OMB expressed concern that our report discusses the development of proposed revisions to EPA's IRIS assessment process, which has not been released for public comment. As we discuss further in comment 10, GAO audits and reviews include those providing prospective analyses of possible or planned agency actions.

3. OMB takes issue with our conclusion that the OMB/interagency review has made it more difficult for EPA to complete IRIS assessments in a timely manner. Our draft and final reports show that the initial OMB/interagency reviews that had been completed as of December 1, 2007, added 6 months or more to the IRIS assessment process. The average length of time for these initial reviews was 7-1/2 months. Given the impact of delays on IRIS assessments and the staff time needed to respond to OMB/interagency comments, we believe such delays are significant. Further, our report discusses five key factors that make it difficult for EPA to complete assessments in a timely manner—one of which is the OMB/interagency review process.

4. OMB states its belief that the draft report is seriously flawed because it does not consider whether interagency reviews improve the quality of IRIS assessments. As OMB notes, our draft report states that we did not evaluate the scientific content or quality of IRIS assessments. However, as the draft and final reports state, the Board of Scientific Counselors—an independent board of experts appointed by EPA to assess its programs—reviewed the effectiveness of the IRIS program (as part of its review of EPA's human health risk assessment program) in November 2007. A report is expected to be finalized in early 2008. In response to our congressional request and to avoid duplication of effort, we focused on the timeliness and credibility of IRIS assessments in the context of the current assessment process and proposed revisions to it. Our draft report also noted that it is too early to determine whether or to what extent the IRIS assessment process changes EPA has implemented in recent years have enhanced the scientific credibility of the assessments—for example, only four assessments were finalized in fiscal years 2006 and 2007. Importantly, because OMB/interagency comments and EPA's response to them are not disclosed, the extent to which the comments added value or caused EPA to revise its risk estimates cannot be determined. However, the status of the IRIS assessment of dibutyl phthalate raises questions about the extent to which the OMB/interagency reviews improve the quality of IRIS assessments. Specifically, this key assessment had cleared both OMB/interagency reviews and was in the

process of being finalized in July 2007. However, because of methodology concerns raised by the Natural Resources Defense Council and the Chairman, Senate Committee on Environment and Public Works, EPA suspended the assessment pending a review by the National Academies.

5. OMB asserts that "the draft report fails to acknowledge that, in the case of documents that involve interagency deliberations, these documents are covered by the deliberative process privilege," and that "accordingly, protection of internal Executive Branch communications is not 'inconsistent with the principle of sound science.'" Contrary to OMB's assertion, the report specifically acknowledges that OMB considers the documents at issue to be protected from disclosure because of their deliberative nature. Moreover, OMB's assertions concerning the deliberative process privilege are misleading and illogical. That is, OMB's comments fail to note that the deliberative process privilege protects internal and interagency communications from judicially compelled disclosure, an issue irrelevant to our report.[1] The privilege in no way prevents agencies from voluntarily disclosing such information.[2] OMB is thus arguing that because the scientific ~~comments at issue might generally be protected from discovery in civil~~ litigation, refusal to disclose them voluntarily in this specific context is necessarily consistent with the principles of sound science. OMB provides no citation or other support for this conflation of judicial and scientific procedures.

   Moreover, OMB's comments that the deliberative process privilege was affirmed in the Freedom of Information Act (FOIA) fails to acknowledge that FOIA requires federal agencies to disclose factual material in documents covered by the deliberative process privilege if the factual material can be reasonably segregated from the deliberative material.[3] OMB's comment appears to assume that because a document passes from one agency to another all of its contents may be withheld from disclosure, a legally unsupportable assertion that courts have uniformly rejected, particularly in the context of attempts to withhold scientific information.[4] Indeed, to the extent that interagency comments on IRIS assessments reflect political and policy concerns rather than discussions of scientific issues, they would be easier to withhold from disclosure in court but harder to justify as part of the IRIS scientific assessment process.

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[1] *NLRB v. Sears, Roebuck & Co.*, 421 U.S. 132, 149 ("it is reasonable to construe Exemption 5 to exempt those documents, and only those documents, normally privileged in the civil discovery context"); *EPA v. Mink*, 410 U.S. 73, 86 (1973) (The Freedom of Information Act (FOIA) contemplates that the public is entitled to all memoranda or letters that a private party could discover in litigation with the agency).

[2] See *Chrysler Corp. V. Brown*, 441 U.S. 281, 293 (holding that exemptions from FOIA's general requirement to disclose agency documents do not prohibit agencies from disclosing information covered by the exemptions). In fact, OMB has voluntarily released information it considered to be protected from disclosure under FOIA, presumably because it saw some benefit in doing so. *NRDC v. U.S. Department of Defense*, 442 F.Supp.2d 857, 863 (C.D. Cal. 2006). It is unclear from the case which FOIA exemptions OMB believed were applicable.

In addition, OMB's comments do not distinguish between risk assessment and risk management decisions, such as the formulation of regulations. As discussed in the draft and final reports, IRIS assessments are not themselves regulations, and OMB and other agencies will have opportunities to engage in deliberative policy debates during, for example, interagency reviews that occur during rule makings. These are points in the process where it is appropriate to address policy questions, such as the implications for other agencies of a specific regulatory decision.

Finally, under the interagency process as currently contemplated, some IRIS assessment reviewers—representatives of federal agencies—essentially are given favored status. OMB fails to explain why certain scientific views should be given added consideration and protected from the critical scientific scrutiny all other comments will receive simply because the reviewers providing the comments are federal employees.

6. OMB stated general disagreement with information presented in our discussion of the naphthalene assessment but did not cite the specific

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[3] E.g., *Mead Data Central, Inc. v. U.S. Dept. of Air Force*, 566 F.2d 242, 260 (D.C. Cir. 1977) ("The focus of the FOIA is information, not documents, and an agency cannot justify withholding an entire document simply by showing that it contains some exempt material.").

[4] E.g., *Bristol-Myers v. FTC*, 424 F.2d 935, 939 (FOIA "does not authorize an agency to throw a protective blanket over all information by casting it in the form of an internal memorandum. Purely factual reports and scientific studies cannot be cloaked in secrecy by an exemption designed to protect only those internal working papers in which opinions are expressed and policies formulated and recommended"); *Southwest Center v. Biological Diversity v. USDA*, 170 F.Supp.2d 931, 943 (D. Ariz. 2000) ("FOIA exemption five does not protect research data"); *Verrazzano Trading Corp. v. United States*, 349 F.Supp. 1401, 1406 (Cust. Ct. 1972) ("the exemption was not intended to protect factual or scientific reports and investigations").

information with which it disagreed. Instead, OMB referred readers to the charge and report from the second peer review EPA had conducted on this chemical at OMB's direction. In our draft and final reports, we report EPA officials' description of the purpose and conclusions of this peer review. Specifically, EPA officials said (1) the agency convened an additional expert review panel on genotoxicity to obtain recommendations about short-term tests that OMB thought could be done quickly and (2) the panel concluded that such research could not be conducted in the short term. The questions posed to the peer reviewers and the summary of results in the report cited by OMB are consistent with EPA's description.

7. OMB says that the draft report is misleading to readers because EPA's "draft document is not a final document." The report clearly identifies the proposed IRIS assessment changes that EPA has been working on. For example, the graphic outlining the proposed changes is titled "EPA's Draft Proposed IRIS Assessment Process." The draft and final reports also state that "as of December 2007, EPA was planning to send a revised draft back to the interagency work group for review and approval." However, to ensure clarity, we have added "draft" prior to our ~~use of the term "proposed process" in a number of places~~.

8. We did not assert that the OMB/interagency process is equivalent to peer review, and we agree with OMB that this review process happens before any external peer review occurs. However, because the OMB/interagency process is opaque, neither peer reviewers nor the public are privy to the changes EPA made to the draft assessments or the charge questions to the peer review panels in response to the comments from OMB and other federal agencies. The presence of transparency at a later stage of IRIS assessment development does not excuse or explain its absence earlier.

9. It is unclear why OMB attempts to rely on the Federal Advisory Committee Act Amendments of 1997 to defend the lack of transparency in the interagency IRIS review process. The transparency procedures applicable to the National Academies' committees to which OMB refers far exceed those that exist under the OMB/interagency IRIS process. For example, under the legislation OMB cites, National Academies' committees must (1) provide the names, biographies, and conflict of interest disclosures of committee appointees; (2) provide an opportunity for the public to comment on the proposed committee member appointments; (3) ensure that meetings focused on data gathering are generally open to the public; (4) provide the names of reviewers of draft committee reports; and (5)

provide summaries of any closed committee meetings. 5 U.S.C. App. 2, § 15. The interagency portion of the IRIS process does none of these things. Moreover, while the act authorizes a National Academies' committee to close meetings at which information exempt from disclosure under FOIA would be discussed, the President of the National Academy of Sciences assured the bill's sponsor, in a letter commenting on the House bill that would later be enacted into law, that the Academy would not rely on the deliberative process exemption as the basis for closing a meeting.

"I wish to assure you that we subscribe fully to the goal of providing as much openness as possible in our work. In particular, we have no intention of using Section 552(b)(5), which deals with interagency memoranda, as a basis for closing meetings of Academy committees. In fact, it is the Academy's standard practice not to treat the type of material covered by Section 552(b)(5) as confidential input to any Academy deliberative process. This procedure insures that, inasmuch as possible, all the information that a committee uses to reach its conclusion is in the public record."

10. We were asked by the Chairman, Senate Committee on Environment and Public Works, to examine the potential effects of planned changes to the IRIS assessment process on EPA's ability to ensure that IRIS provides current, credible risk information. This review therefore involved evaluating a draft of EPA's planned IRIS assessment changes. GAO audits and reviews include those providing prospective analyses of possible or planned agency actions. We may also assess the ability of alternative approaches to yield better program performance or eliminate factors that inhibit program effectiveness. As is typical in cases in which we evaluate draft proposals, we make our recommendations on the IRIS assessment process in the spirit of informing those revisions.

Appendix VI: GAO Contact and Staff Acknowledgments

GAO Contact	John B. Stephenson, (202) 512-3841 or stephensonj@gao.gov
Staff Acknowledgments	In addition to the contact named above, Christine Fishkin (Assistant Director), Mark Braza, Nancy Crothers, Laura Gatz, Richard P. Johnson, Summer Lingard, Susan Swearingen, and Delia Zee made key contributions to this report. Also contributing to this report were Tim Bober, Phylis Cline, Michael Derr, and Cynthia Taylor.

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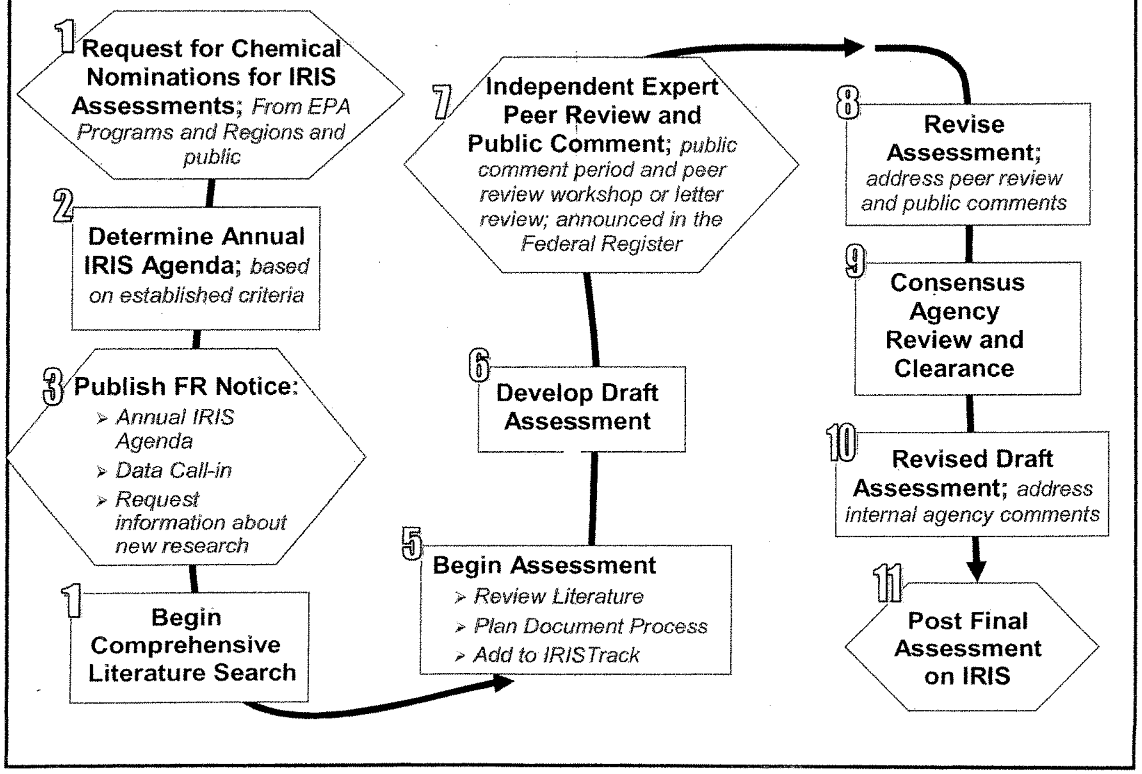
IRIS PROCESS: Pre-2004



1 **Request for Chemical Nominations for IRIS Assessments;** *From EPA Programs and Regions and public*

2 **Determine Annual IRIS Agenda;** *based on established criteria*

3 **Publish FR Notice:**
- *Annual IRIS Agenda*
- *Data Call-in*
- *Request information about new research*

1 **Begin Comprehensive Literature Search**

5 **Begin Assessment**
- *Review Literature*
- *Plan Document Process*
- *Add to IRISTrack*

6 **Develop Draft Assessment**

7 **Independent Expert Peer Review and Public Comment;** *public comment period and peer review workshop or letter review; announced in the Federal Register*

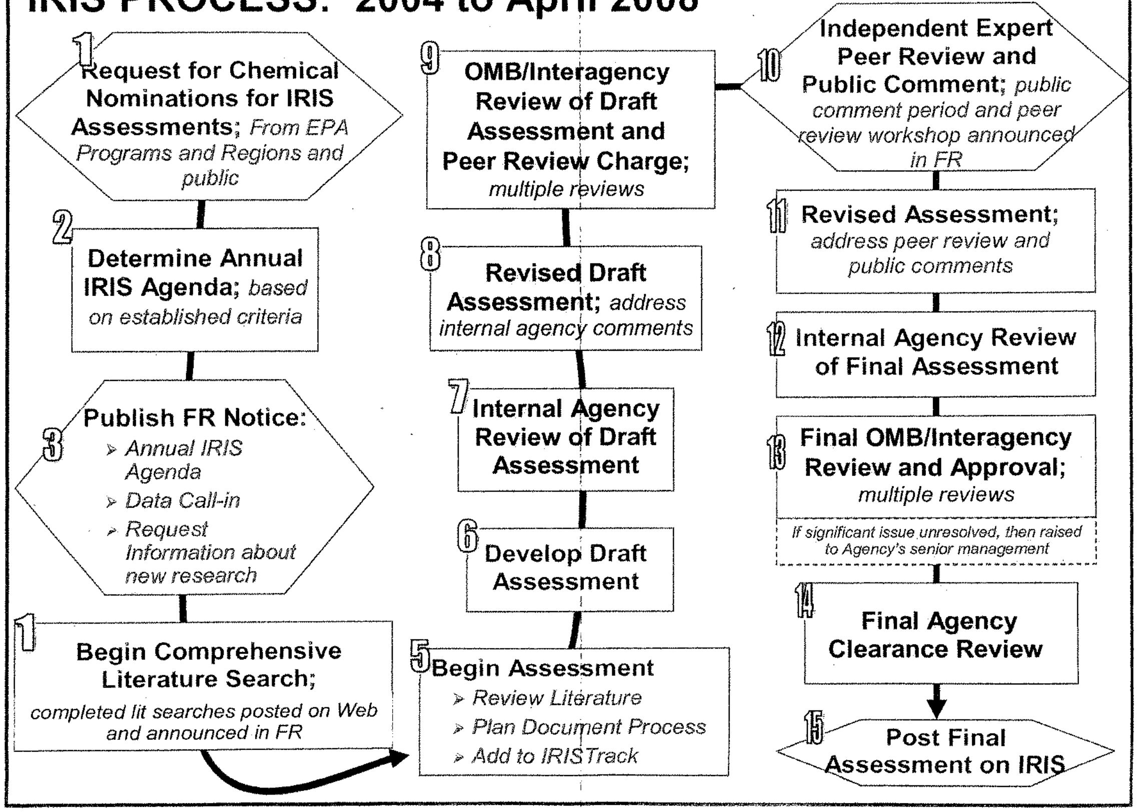
8 **Revise Assessment;** *address peer review and public comments*

9 **Consensus Agency Review and Clearance**

10 **Revised Draft Assessment;** *address internal agency comments*

11 **Post Final Assessment on IRIS**

IRIS PROCESS: 2004 to April 2008



1 **Request for Chemical Nominations for IRIS Assessments;** *From EPA Programs and Regions and public*

2 **Determine Annual IRIS Agenda;** *based on established criteria*

3 **Publish FR Notice:**
- *Annual IRIS Agenda*
- *Data Call-in*
- *Request Information about new research*

4 **Begin Comprehensive Literature Search;** *completed lit searches posted on Web and announced in FR*

5 **Begin Assessment**
- *Review Literature*
- *Plan Document Process*
- *Add to IRISTrack*

6 **Develop Draft Assessment**

7 **Internal Agency Review of Draft Assessment**

8 **Revised Draft Assessment;** *address internal agency comments*

9 **OMB/Interagency Review of Draft Assessment and Peer Review Charge;** *multiple reviews*

10 **Independent Expert Peer Review and Public Comment;** *public comment period and peer review workshop announced in FR*

11 **Revised Assessment;** *address peer review and public comments*

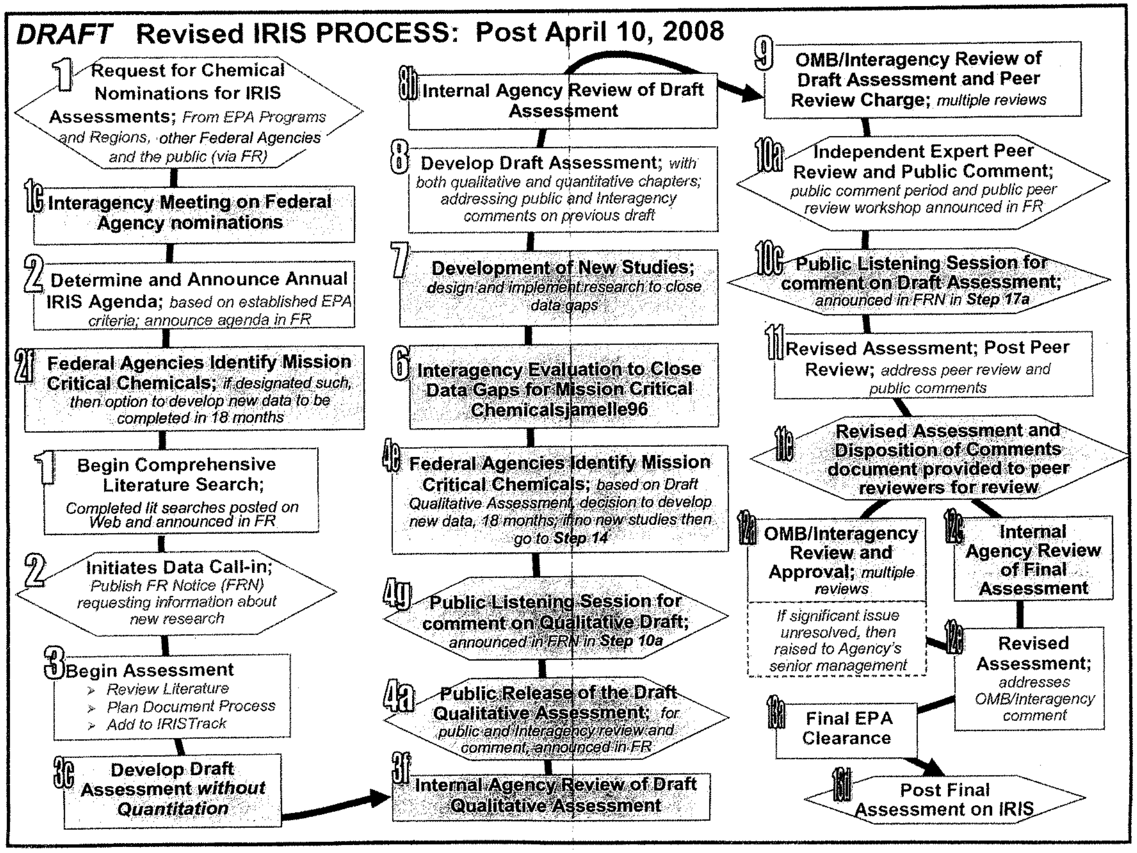
12 **Internal Agency Review of Final Assessment**

13 **Final OMB/Interagency Review and Approval;** *multiple reviews*

If significant issue unresolved, then raised to Agency's senior management

14 **Final Agency Clearance Review**

15 **Post Final Assessment on IRIS**


DRAFT Revised IRIS PROCESS: Post April 10, 2008
1
Request for Chemical Nominations for IRIS Assessments; From EPA Programs and Regions, other Federal Agencies and the public (via FR)
1c
Interagency Meeting on Federal Agency nominations
2
Determine and Announce Annual IRIS Agenda; based on established EPA criteria; announce agenda in FR
2f
Federal Agencies Identify Mission Critical Chemicals; if designated such, then option to develop new data to be completed in 18 months
1
Begin Comprehensive Literature Search; Completed lit searches posted on Web and announced in FR
2
Initiates Data Call-in; Publish FR Notice (FRN) requesting information about new research
3
Begin Assessment
➢ Review Literature
➢ Plan Document Process
➢ Add to IRISTrack
3c
Develop Draft Assessment without Quantitation
3f
Internal Agency Review of Draft Qualitative Assessment
4a
Public Release of the Draft Qualitative Assessment; for public and Interagency review and comment, announced in FR
4g
Public Listening Session for comment on Qualitative Draft; announced in FRN in Step 10a
4e
Federal Agencies Identify Mission Critical Chemicals; based on Draft Qualitative Assessment, decision to develop new data, 18 months; if no new studies then go to Step 14
6
Interagency Evaluation to Close Data Gaps for Mission Critical Chemicalsjamelle96
7
Development of New Studies; design and implement research to close data gaps
8
Develop Draft Assessment; with both qualitative and quantitative chapters; addressing public and Interagency comments on previous draft
8b
Internal Agency Review of Draft Assessment
9
OMB/Interagency Review of Draft Assessment and Peer Review Charge; multiple reviews
10a
Independent Expert Peer Review and Public Comment; public comment period and public peer review workshop announced in FR
10c
Public Listening Session for comment on Draft Assessment; announced in FRN in Step 17a
11
Revised Assessment; Post Peer Review; address peer review and public comments
11c
Revised Assessment and Disposition of Comments document provided to peer reviewers for review
12a
OMB/Interagency Review and Approval; multiple reviews
If significant issue unresolved, then raised to Agency's senior management
12c
Internal Agency Review of Final Assessment
12e
Revised Assessment; addresses OMB/Interagency comment
13a
Final EPA Clearance
13b
Post Final Assessment on IRIS

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

APR 10

Apr 10, 2008

DEPUTY ADMINISTRATOR

MEMORANDUM

FROM: Marcus Peacock Marcus Peacock

TO: George Gray
Assistant Administrator, ORD

SUBJECT: Implementation of Revised IRIS Process

I understand that the Agency has completed its review of the IRIS process. The revised process is described in the document entitled "*EPA's Integrated Risk Information System: Assessment Development Procedures*" (attached). As you are aware, reforming the IRIS process has been an important goal of the Administrator, as reflected in his Action Plan.

I believe that the revised IRIS process will provide greater transparency, objectivity, balance, rigor and predictability in IRIS assessments. For example, the revised process creates a new step that allows the public to bring forth additional scientific information and to comment on the scope of an assessment early in the IRIS process. New opportunities are also provided for EPA to host a "listening session" during public review and comment periods to allow for broader participation and engagement of interested parties. Additionally, the revised process creates a limited opportunity for other agencies to collect data to fill significant data gaps for "mission critical" chemicals. Although interagency comments on IRIS assessments are considered deliberative in nature (as is the case for all EPA assessments), all conclusions reached by the Agency, including justifications for making science or science policy decisions, are made available to interested parties and the public in the assessment and all IRIS assessments undergo a thorough peer review. Final decisions on the content of IRIS assessments clearly remain with EPA.

These and other improvements to the IRIS process help to define critical and appropriate roles for public and interagency comments and interactions, and promote and foster greater communication and sharing of information between interested parties and EPA. I believe that the outcome of these improvements will be a more predictable, streamlined, and transparent process for conducting IRIS assessments, which will ultimately lead to assessments that are of the highest quality and rigor. The revised process is also expected to result in a much more timely completion of IRIS assessments than has occurred in the past.

The Administrator gave us this task three years ago. Given this and the many advantages the revised process holds relative to past or current practices, the Agency should begin following the steps outlined here as soon as possible. Consequently, I request that you implement the new

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IRIS process in all ongoing and future scientific and science-policy assessments, effective immediately. This process, however, should be seen as a "living" document that can be revised and improved as experience is gained and new ideas brought forward. I encourage you to share this process widely and encourage review and comment from interested parties.

The revised IRIS process will yield assessments that are of the highest quality and timeliness, so that they can be used by the Agency, States, the public and various other stakeholders. I look forward to continuing to work with you to advance the Agency's goals through this important process.

Attachment

EPA's Integrated Risk Information System

Assessment Development Procedures

Introduction: The Integrated Risk Information System (IRIS) is a U. S. Environmental Protection Agency (EPA) database that contains the Agency's science and science policy positions on chronic human health effects that may result from exposure to environment contaminants. Through IRIS, EPA provides the highest quality science-based human health assessments to support Agency policymaking activities.

Since the 1980s when IRIS began, EPA has taken many steps to improve the IRIS process that make it more accessible and transparent. In addition, the Agency has worked to enhance the independent expert peer review process to assure high quality human health assessments. In its continuing efforts to improve risk assessment practices, EPA has reviewed its development processes for human health assessments that, once completed, are included on IRIS.

The role of other Federal agencies and the public in the IRIS process is to promote communication, sharing of information, and teaming with EPA at key points throughout the nomination and assessment activities. Agencies may identify chemical substances that are critical to their mission and operation, therefore initiating targeted discussions with EPA in the development of risk assessments for these mission critical chemicals. The public is also offered opportunities to bring forth data and expertise to inform the IRIS process. The enhanced transparency brought about by teaming of other Federal agencies and the public with EPA will help identify scientific issues early, which will ultimately help streamline the IRIS process.

I. Annual Chemical Nomination Process

1. EPA Initiates Annual Nomination Process for IRIS Assessments (75 days)

A. EPA's Office of Research and Development (ORD) issues a *Federal Register* (FR) notice inviting public nominations of chemical substances for ORD to consider for inclusion on the IRIS Program annual agenda (Agenda). Nominations could include chemical substances to consider for the development of new assessments as well as the revision of assessments already on IRIS for which critical new information is available. Nominations must be submitted within 60 days of the solicitation.

B. Simultaneously, ORD asks the EPA Program and Regional Offices and other agencies to nominate chemical substance(s) for inclusion on the Agenda.

   a. Agencies include, but are not limited to, HHS, NASA, DOA, DOE, DOT, DOD, OMB, CEQ, and OSTP.

   b. Each interested agency appoints one point of contact (POC) at the organizational level it deems appropriate. Each agency POC is responsible for keeping their management appropriately informed and for coordinating reviews of draft IRIS documents by that agency.

   c. ORD appoints the POC in the IRIS program.

   d. ORD notifies EPA Program and Regional Offices via memorandum to the EPA Deputy Assistant Administrators and Deputy Regional Administrators, with a copy to the intra-Agency IRIS Review Committee (via email), about the request for assessment nominations.

  e. ORD notifies the other agencies via memorandum to the agency POCs (via email) about the request for assessment.
  f. Other agencies and EPA Program and Regional Offices have 60 days to submit nominations for inclusion on the Agenda; nomination submittals will be considered part of the public record.
  g. If an other agency or EPA Program and Regional Office does not respond within 60 days of the solicitation ORD will assume that it did not have any nominations for that year.
  h. Other agencies and EPA Program and Regional Offices provide documentation that supports their interest in the chemical(s) and rationale for consideration to ORD.

C. At the end of the nomination period, within 15 days, ORD calls a meeting with other agencies and EPA Program and Regional Offices to discuss their nominations, including:
  a. Other agencies' or EPA's Program and Regional Offices' specific questions and concerns about, and recommendations for, adding or updating assessments for the chemical substance(s) that they nominate;
  b. The importance that other agencies or EPA Program and Regional Offices place on having the chemical substance(s) that they nominate included on the Agenda, and the basis for the nomination; and
  c. Current or planned research and/or assessments by EPA or the other agencies.

2. EPA Determines Annual IRIS Agenda (30 – 60 days)

A. ORD applies its published selection criteria to the slate of nominated chemicals.

B. ORD reviews its available work force and areas of expertise that might be available for new assignments.

C. ORD prepares the IRIS Program Annual Agenda, which lists the chemical substances for which work will be initiated in the upcoming year, including chemicals selected by ORD and consideration of chemicals nominated in response to **Step 1.A** and **Step 1.B**.

D. ORD notifies EPA Program and Regional Offices, other agencies, and the public that the IRIS Program Annual Agenda is available.
  a. Notify EPA Program and Regional Offices by memorandum to the EPA Deputy Assistant Administrators and Deputy Regional Administrators, with a copy to the intra-Agency IRIS Review Committee (via email).
  b. Notify other agencies by memorandum to agency POCs (via email).
  c. Notify public by issuing an FR notice announcing the IRIS Program Annual Agenda (new starts and updates).

E. The other agencies or EPA Program and Regional Offices may decide at this early stage to sponsor or perform research associated with the chemicals selected or proposed to be assessed if they conclude that such work would be beneficial to the assessment or future re-assessments. The results of this research will be considered for inclusion in the IRIS assessment if it is completed within an appropriate time frame as determined by ORD and has undergone independent external peer review (e.g., peer review publications or independent peer review panel evaluations).

F. The other agencies identify to ORD an initial list of the chemical(s) on the IRIS Program Annual Agenda that they have determined meet the definition of mission critical [1].

II. The Assessment Process

1. EPA Conducts Scientific Literature Search (60 – 90 days)

A. ORD appoints a chemical manager(s) for each chemical on the IRIS Program Annual Agenda.

B. The chemical manager(s) direct an EPA contractor to conduct and complete a comprehensive search of the scientific literature for the chemical.

2. EPA Initiates Data Call-In (45 – 60 days)

A. After the literature search has been completed for each chemical, ORD publishes an FR notice that notifies the public that completed literature searches for a set of chemicals are available on the IRIS Internet site, and invites the public and other agencies to submit additional scientific information (studies, reports, other assessments, etc.) on the chemical.

  a. FR notice requests information on new research that may be planned, underway, or in press.

  b. FR notice includes notification that the initial literature review results for each chemical are available on the Internet for review (eliminates submission of information about which EPA is already aware).

  c. FR notice includes information on how and where to submit scientific information.

  d. A minimum of 45 days is provided for submission of information.

B. ORD ensures that EPA Program and Regional Offices and other agencies are aware of the FR notice:

  a. EPA Program and Regional Offices: via email

  b. Other agencies: via email to agency POCs. Each agency POC is responsible for keeping his/her management appropriately informed.

C. Other agencies confirm to ORD whether the chemical is mission critical. It is expected that only a few chemicals will receive this designation.

---

[1] A mission critical chemical is one that is an integral component to the successful and safe conduct of an Agency's mission in any or all phases of its operations. Impacts on use of mission critical chemicals include cessation or degradation of the conduct of the mission and/or unacceptable resource constraints.

3. EPA Begins IRIS Assessment and Develops Draft Qualitative Assessment (180 – 240 days)

A. ORD identifies and assembles an IRIS assessment team.

B. ORD reviews new scientific information submitted in response to the call for information in **Step 2.**

C. ORD assesses the data in the scientific literature and submitted in **Step 2** and develops a draft Qualitative Assessment for the chemical being assessed, including:

  a. summary of potentially important health effects;

  b. summary of information on potential mode(s) of action;

  c. summary of information about potentially susceptible populations;

  d. description of approaches being considered for dose-response assessment including default approaches and types of models under consideration;

  e. identification and discussion of potential uncertainty factors; and

  f. identification of potential uncertainties that impact the qualitative and quantitative aspects of the assessment.

D. This draft Qualitative Assessment does not include quantification; however, extensive qualitative information including ORD's interpretation of scientific data and description of potential assumptions and approaches will be included.

E. The draft Qualitative Assessment completes internal ORD clearance.

F. The draft Qualitative Assessment completes internal EPA review via the intra-Agency IRIS Review Committee. Intra-Agency comments are deliberative.

4. EPA Initiates Public and Agency Review of Draft Qualitative Assessment (45 – 60 days)

A. ORD issues a FR notice inviting the public and other agencies to comment on the draft Qualitative Assessment.

B. On the publication date of the FR notice, the draft Qualitative Assessment is posted on the IRIS Internet site.

C. ORD ensures that EPA Program and Regional Offices and other agencies are aware of the FR notice.

D. The FR notice includes instructions for submitting comments to ORD. The FR notice also requests that the public and other agencies identify missing types of studies and areas where uncertainties might be reduced, modes of action elucidated, or estimation of dose-response informed through new short-term (12 month) research.

E. Other agencies may identify a chemical as mission critical based on the results of the draft Qualitative Assessment (see Annual Chemical Nomination Process - **Step 2.F**).

F. All public comments received during the official public comment period must be submitted through E-Gov (www.regulations.gov); all public comments will be part of the official record. Other agency comments are deliberative.

G. ORD holds a "listening session" during the public review process to allow all interested parties to comment on the draft Qualitative Assessment.

5. EPA Initiates Review of Public and Agency Comments (30 days)

A. ORD compiles and reviews all public and other agency comments received on the draft Qualitative Assessment, and shares the comments with EPA Program and Regional Offices and other agencies.

B. ORD provides other agencies and EPA Program and Regional Offices with information about any significant changes that might occur in the IRIS assessment as a result of the public or other agency comments and listening session.

C. If another agency or the public wants to discuss with ORD a particular comment or set of comments, they should contact the IRIS POC to arrange a meeting with ORD.

D. If significant alternative science or science policy judgments are raised by the public, EPA Program or Regional Offices, or other agencies, these will be added to the document and brought forward in the charge to the independent external peer review panel.

6. Evaluation of Agency Interest in Closing Data Gaps for Mission Critical Chemicals (90 days)

A. If another agency is interested in filling a significant data gap, it must first document that the chemical is mission critical (see Annual Chemical Nomination Process - **Step 2.F** and The Assessment Process - **Step 4.E**).

B. For mission critical chemicals, the agency interested in addressing data gaps will consider the comments provided in **Steps 4 and 5**, and submit to ORD a research plan that documents how the conduct of new research has the potential to reduce uncertainties, clarify the mode-of-action, or inform the estimation of dose-response. The other agency must also show that the proposed research and peer review can be completed in less than 18 months. If desired, a letter of agreement between ORD and the other agency sponsoring the research can be created articulating the relevance of the proposed research to the risk assessment and how the proposed research may inform the risk assessment. Such a letter would indicate the timeframe for expected research to be completed.

C. The sponsoring agency may decide that an independent 3rd party consultation should be done to evaluate the estimated costs of the proposed research, and the expected benefits of additional research for the assessment. This 3rd party consultation must be completed during this 90 day period.

D. If a sponsoring agency wants to partner with an external party or any other agency to conduct a study, that decision is theirs to make, but ORD and other interested agencies should be informed.

E. If no request for developing new short-term research is received, or if no interest in conducting such research is expressed for mission critical chemicals, proceed to **Step 8.**

7. Design and Implementation of New Studies for Mission Critical Chemicals (365 – 540 Days)

A. If in **Step 6** the consequences and interest in closing data gaps are determined to be critical by ORD, in consultation with the intra-Agency IRIS Review Committee and other interested agencies, the agency can sponsor the new research.

B. ORD will generally allow no more than an 18 month hiatus from the completion of the IRIS assessment to allow for the completion and peer review of studies specified in **Step 6**.

C. The sponsoring agency develops a detailed research plan and solicits comments and recommendations on the research plan from ORD, in consultation with the intra-Agency IRIS Review Committee, and from other agencies. ORD and the other agencies respond to the sponsoring agency within 30 days, focusing on study design and whether the research, if conducted as planned, is likely to reduce uncertainties (e.g., specific uncertainty factor), clarify the mode-of-action, or inform the estimation of dose-response. The study plan and characterization of potential impacts on the assessment is documented in a letter between the sponsoring agency and ORD, as a complement to the letter discussed in **Step 6.B**.

D. The agency sponsoring the research will work expeditiously to complete its planning, protocol design, and study implementation. ORD, in consultation with the intra-Agency IRIS Review Committee, will provide timely reviews and responses of any aspect of this work, if requested by the sponsoring agency.

E. If ORD or the sponsoring agency deems that consultations are warranted, ORD or the sponsoring agency can call meetings and teleconferences to discuss critical issues articulated in correspondence among the agencies. Third-party consultants can be invited by ORD or the other agencies to participate in these meetings and teleconferences.

F. An agency may also sponsor or perform any other research (that is outside the scope of this effort) associated with the chemical being assessed if it concludes that such work might be beneficial to a future IRIS assessment. Agencies will continue to direct their internal research agendas as they see fit.

G. The sponsoring agency provides the study report(s) to ORD and other interested agencies immediately upon completion of the study.

H. Independent External Peer Review (included as part of **Step 7** timeframe):

   a. Upon completion of the study, the sponsoring agency arranges for external peer review of the research report(s) by the scientific community.

   b. The sponsoring agency consults with ORD in determining who will conduct this review, the level of review, and by what means (e.g., panel review).

   c. ORD and the sponsoring Agency provide the studies, peer review comments and disposition of comments report(s) to the public.

   d. If ORD or the sponsoring agency deems that consultation is warranted, ORD or the sponsoring agency may call a meeting to discuss critical issues and significant disagreements about the peer reviews. Third-party consultants may be invited by ORD or the sponsoring agency to participate in this meeting.

I. ORD, in consultation with the intra-Agency IRIS Review Committee, will consider the results of the new studies carefully as it proceeds with the development of the assessment. Discussion of the new study results will be included in the draft assessment.

8. EPA Completes Draft IRIS Toxicological Review (120 – 270 days)

A. ORD completes the draft IRIS Toxicological Review.

   a. The draft IRIS Toxicological Review draws upon the previous draft Qualitative Assessment and the comments received in **Steps 4 and 5.**

   b. ORD reviews and analyzes any new short-term research completed under **Steps 6 and 7.**

   c. The draft IRIS Toxicological Review includes a quantitative assessment, including application of uncertainty factors, mode-of-action information, and dose-response modeling.

B. The draft IRIS Toxicological Review undergoes internal ORD review (30 – 45 days).

C. ORD submits the draft IRIS Toxicological Review for internal review via the intra-Agency IRIS Review Committee and addresses intra-Agency comments (30 – 60 days).

D. Determination of peer review characteristics:

   a. For mission critical chemicals, ORD will cooperate with other interested agencies to determine the level of peer review (e.g., National Academy of Science (NAS) review, EPA Science Advisory Board (SAB) review, or contractor-led panel peer review), panel disciplines, and the scope of the review.

   b. For other chemicals, ORD determines the level of peer review, panel disciplines, and the scope of the review.

   c. ORD develops any contract documentation.

9. EPA Initiates Interagency Review of Draft IRIS Toxicological Review (45 – 105 days)

A. ORD sends the draft IRIS Toxicological Review and draft external peer review charge questions to OMB to initiate interagency review.

B. ORD develops a charge for interagency reviewers. It is anticipated that the interagency review charge will remain similar for each draft IRIS Toxicological Review, with chemical specific text added as appropriate.

C. OMB distributes the draft IRIS Toxicological Review, draft external peer review charge questions, and the interagency review charge to interagency reviewers.

   a. Length of review period is 30 – 60 days and depends on complexity of draft assessment documents.

   b. OMB facilitates interagency review to help assure timely response within designated review period.

D. OMB compiles and provides all interagency comments to ORD; other agency comments are deliberative.

   a. ORD assumes "no comment" from other agencies that do not respond within the designated review period.

   b. If another agency requests an extension of the review period, both the IRIS POC and OMB POC should be contacted regarding the request and the justification.

E. ORD addresses the interagency comments and develops a "disposition of comments" document and revises the draft assessment documents, as appropriate, within 15 – 30 days.

F. Within 15 days after the comment period ends, ORD, OMB, or other interested agencies may call a meeting to discuss and resolve critical issues and significant disagreements articulated in the other agencies' comments on the draft assessment documents.

  a. OMB serves as the facilitator for the meeting.
  b. Areas of disagreement may result in additional charge questions for the external peer review.

10. EPA Initiates Independent External Peer Review and Releases External Draft IRIS Toxicological Review (120 – 280 days[2])

A. ORD provides the draft IRIS Toxicological Review and peer review charge questions to independent external peer reviewers. Peer reviews are public meetings, generally through a face-to-face meeting of panelists, though some may be held via public teleconference.

B. Concurrently, ORD publicly releases the draft IRIS Toxicological Review and charge to peer reviewers for public review and comment on the IRIS Internet site.

  a. ORD prepares an FR notice announcing a public comment period of 45 to 60 days.
  b. Length of the public comment period depends on the complexity of the draft IRIS Toxicological Review.
  c. The draft IRIS Toxicological Review and charge to peer reviewers is released on the IRIS Internet site on the day that the FR is published.
  d. Public comment period is open to all stakeholders, including other agencies.
  e. ORD insures that other agencies are aware of the FR notice.

C. ORD holds a "listening session" during the public comment process to allow all interested parties to comment on the draft IRIS Toxicological Review.

D. Public comments from Steps B and C are submitted to ORD.

  a. All public comments received during the official public comment period will be submitted through E-Gov (www.regulations.gov); all public comments will be part of the official record.
  b. Comments received by the close of the public comment period will be provided to the external peer review panel at least 30 days in advance of the peer review meeting.

E. The report of the external peer review panel becomes part of the public record for the IRIS assessment.

11. EPA Revises IRIS Toxicological Review and Develops IRIS Summary (120 – 150 days)

A. ORD evaluates the external peer review panel report and public comments.

B. ORD revises the draft IRIS Toxicological Review, as appropriate, and develops the IRIS Summary.

C. Length of revision process depends on the complexity of the IRIS Toxicological Review and complexity and number of peer reviewer and public comments.

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[2] This time frame does not include reviews conducted by the National Academy of Sciences (NAS).

D. Within 90 – 120 days, ORD develops a disposition of peer reviewer and public comments and provides the disposition of comments document and the revised IRIS Toxicological Review and IRIS Summary to the external peer review panel members for their comment within 30 days.

E. ORD provides the disposition of peer reviewer and public comments document and any additional peer review panel comments from **Step 11.D** as an appendix to the IRIS Toxicological Review.

12. EPA Initiates Final Agency and Interagency Review of the IRIS Toxicological Review and IRIS Summary (30 – 45 days)

A. ORD sends the final IRIS Toxicological Review and IRIS Summary to OMB for distribution to the other agencies.

B. In general, this distribution is intended as a final check-in to address any remaining issues and ensure that public and peer reviewer comments were adequately considered or addressed by ORD.

C. Concurrently, ORD sends the IRIS Toxicological Review and IRIS Summary to the intra-Agency IRIS Review Committee for comment (30 days).

D. OMB compiles and provides all interagency comments to ORD within 30 days.

   a. ORD assumes "no comment" if the other agencies or EPA Program or Regional Offices do not respond within the designated review period.

   b. If another agency or EPA Program or Regional Office requests an extension of the review period, both the IRIS POC and OMB POC should be contacted regarding the request and the justification.

E. ORD addresses and resolves any remaining issues in consultation with OMB and other agency or EPA Program or Regional Office POCs within 15 days. Should resolution of any issue not be achieved in discussions with the POC, the other agency or EPA Program or Regional Office that raised the issue may decide to elevate the discussion to their senior management level to achieve resolution. The final decision on IRIS content remains with EPA.

13. EPA Completion of IRIS Toxicological Review and IRIS Summary (60 days)

A. ORD completes the IRIS Toxicological Review and IRIS Summary.

B. ORD prepares the final assessment to post on the IRIS Internet site.

C. ORD insures 508 Compliance and EPA web site compliance.

D. ORD posts the assessment to the IRIS Internet site. ORD completes and maintains the public record.

American® Chemistry Council

SHARON H. KNEISS
VICE PRESIDENT
PRODUCTS DIVISIONS

Via Courier

May 3, 2007

George M. Gray, Ph.D.
Assistant Administrator for Research and Development
United States Environmental Protection Agency
Mail Code 8101 R
1201 Constitution Avenue, N.W.
Washington, D.C. 20004

Dear Dr. Gray:

Re: IRIS Peer Review of Polybrominated Diphenyl Ethers (PBDEs)
Docket ID No. EPA-HQ-ORD 2006-0838

I am writing to convey the serious concerns of the Brominated Flame Retardant Industry Panel ("BFRIP" and "the Panel") of the American Chemistry Council (ACC)[1] regarding the ongoing toxicological assessment of PBDEs. We have particular concern with the assessments for decabromodiphenyl ether ("deca-BDE"), which is being performed by the U.S. Environmental Protection Agency ("EPA" or "the Agency") to update the Integrated Risk Information System (IRIS). BFRIP requests that you review its concerns and take steps to ensure the independence and objectivity of EPA's IRIS reassessment.

I. EXECUTIVE SUMMARY

- BFRIP is concerned about both the composition of and process for forming the Agency's external peer review panel, especially by the appearance that the peer review panel's leadership might lack the impartiality and objectivity necessary to conduct a fair and impartial review of the data.
- When recommending a revised reference dose (RfD) for deca-BDE, the external peer review panel (and EPA) appear to be ready to rely on a study that fails to meet the Agency's standards for accurate and reliable data. The study is based

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[1] BFRIP is under ACC's Chemical Products and Technology Division and its members are the U.S. manufacturers and importers of brominated flame retardants: Albemarle Corporation, AmeriBrom, Inc., and Chemtura Corporation (collectively "the Panel").

upon a design that does not conform to Agency guidelines and was not performed in accordance with Good Laboratory Practices ("GLP").

- BFRIP urges the Agency to reject any recommendations to combine the PBDEs as a group for purposes of the revised IRIS evaluation, because this is contrary to the data within the Agency's possession and would not conform with established principles of toxicology. Each of the PBDEs and deca-BDE in particular must be evaluated on its own very robust database and the comprehensive weight of the evidence.

II. BACKGROUND AND INTRODUCTION

These concerns are of sufficient import to merit your attention. BFRIP has a long-standing tradition of working closely and cooperatively with the Agency to generate and assess data concerning the brominated flame retardants. To that end, BFRIP has submitted countless studies to the Agency (and to international bodies) and has participated in numerous Agency data-development and risk assessment programs, such as the High Volume Production ("HPV") Challenge Program and the Voluntary Children's Chemical Evaluation Program ("VCCEP"). Panel members also have demonstrated a strong commitment to working collaboratively with the Agency on a variety of policy and programmatic issues, including the development of a product stewardship program specifically for down-stream users of the various brominated flame retardant products BFRIP's members produce. In addition, the manufacturers which comprise BFRIP also sponsor another stewardship program called the Voluntary Emissions Control Action Programme ("VECAP") which was established to manage, monitor and minimize industrial emissions of brominated flame retardants through partnership with the supply chain.

Because of its close working relationship with EPA and other regulatory agencies, the Panel is compelled to formally raise its specific concerns regarding the process followed for the IRIS PBDE External Peer Review, including the reliability of the data being assessed, the integrity of the peer review process, and certain information that has come to light that could suggest the potential for bias exists on the part of the Peer Review Chairperson. In addition, the Panel has specific concerns regarding technical aspects of the Final Report of the External Peer Review published on April 4, 2007[2] ("Final Report") that will be addressed in greater detail below.

The Panel members request that you personally review BFRIP's concerns and take appropriate actions before the draft Toxicological Review is issued in final form. The importance of the IRIS Review cannot be underestimated because the IRIS data base is relied upon by various EPA offices and numerous other bodies, including federal and state regulatory agencies; thus, it is imperative that the IRIS reassessment be based upon credible information. Therefore, the Panel is willing to work with EPA in a timely fashion to provide any additional comments, information, and support as needed to arrive at a final Review that meets the rigorous standards of scientific integrity and data quality that appropriately are expected of the Agency and are required by the Information Quality Act for influential government documents such as EPA's own publications and the IRIS system in particular.

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[2] *See* http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=161970.

III. THE PANEL'S CONCERNS REGARDING THE PEER REVIEW PROCESS

The Agency's Peer Review Handbook (3rd ed.) ("Handbook") provides a comprehensive overview of the Agency's expectations concerning the peer review process and the steps necessary to ensure transparency and accountability as required by the Office of Management and Budget's ("OMB") Final Information Quality Bulletin for Peer Review. Central to every peer review, but of particular importance here, is the Handbook's guidance on assembling and convening a peer review panel and the necessary steps that must occur before embarking on the substantive review of the underlying technical materials. Unfortunately, it is not clear that such considerations were addressed adequately by the Agency when initiating the External Peer Review for the IRIS-PBDE Toxicological Review.

A. EPA Did Not Solicit Appropriate Input As Suggested by Agency Policies

EPA's Handbook states that the

> [s]election of peer reviewers should be made by identifying reviewers with the appropriate expertise and then narrowing the field of potential peer reviewers to those individuals that are independent, do not have a conflict of interest and do not appear to lack impartiality. You should also consider requesting that the public, *including scientific and professional societies*, nominate peer reviewers.

Handbook, §§3.4.1-3.4.2 at 60-61 (emphasis added); *see also* "Advisory Committee Meetings and Report Development: Process for Public Involvement" available at http://www.epa.gov/sab/pdf/sabso_04_001.pdf (stating that "[a]gency policy . . . not only allow[s] but also encourage[s] public involvement"). In the case of the PBDEs External Peer Review, the public, including well-positioned and knowledgeable scientific groups such as BFRIP, were not asked to nominate reviewers. *See* Peer Review Plan for DRAFT IRIS HEALTH ASSESSMENT OF 2,2',4,4'-TETRABROMODIPHENYL ETHER (BDE-47) CASRN 5436-43-1 2,2',4,4',5-PENTABROMODIPHENYL ETHER (BDE-99) CASRN 60348-60-9 2,2',4,4',5,5'-HEXABROMODIPHENYL ETHER (BDE-153) CASRN 68631-49-2 2,2',3,3',4,4',5,5',6,6'-DECABROMODIPHENYL ETHER (BDE-209) CASRN 1163-19-5. Indeed, BFRIP could have provided the drafters with valuable information and insight concerning potential peer reviewers.

Further, pursuant to government-wide and EPA directives, a Peer Review Plan for influential scientific information must be made available for public comment. *See* Handbook, §1.4.3 at 21. Without any formal comment period or published docket specific to the Peer Review Plan, BFRIP was not provided an adequate opportunity to comment on the Plan. If it had, the Panel members would have encouraged EPA to open up peer reviewer nomination process to include all relevant stakeholders.

B. The External Peer Review for PBDEs Does Not Appear to Be an "Independent, Third-Party Review"

According to EPA's own Handbook,

> [t]he goal of peer review is to obtain an independent, third-party review of the product from experts who have not substantially contributed to its development. *When experts have a material stake in the outcome of the peer review . . . or have participated* *__substantially__* *in the development of the product, those experts' reviews may not qualify as unbiased, independent peer review . . . .*

Handbook, §1.2.5 at 13 (emphasis added). Thus, the selection of independent peer reviewers is critical and "EPA should always make every effort to use peer reviewers who do not have any conflict of interest or appearance of a lack of impartiality, and who are completely independent." *Id.*, §3.4.1 at 60.

While the definition of an "appearance of a lack of impartiality" may vary somewhat depending on the status of a peer reviewer[3], the basic concept is the same for all reviewers -- that is, a peer reviewer should not be or have been engaged in activities, or have an interest, that would lead a reasonable person to believe that the peer reviewer is biased or predisposed to favor one view over another. *See, e.g.,* 5.C.F.R. §2635.502(a). Indeed, EPA even recommends asking potential peer reviewers specific questions to determine whether there is an "appearance" issues, such as:

- Have you made any public statements (written or oral) on the issue? and;
- Have you made any public statements that would indicate to an observer that you have taken a position on the issue under consideration?

Handbook, §3.4.5 at 67. Making such inquiries in context of the PBDEs Review would have revealed issues that appear not to have been addressed.

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[3] External peer review can be conducted by individual experts who are either Regular Government Employees (RGEs) of another agency, experts hired as EPA Special Government Employees (SGEs), or experts who are retained through a contractual process. *See* Handbook, §3.4.5. at 60. The employment status of the PBDE peer reviewers is unknown to BFRIP.

With regard to the PBDE External Peer Review, BFRIP submits that genuine "appearance" issues exist relating to independence and objectivity of the peer review panel Chairperson. Earlier this year, the Chairperson testified before the Maine legislature, on behalf of the Maine Center for Disease Control and Prevention, specifically advocating that the state mandate a phase out of deca-BDE. The proposal included a sales ban on televisions and other consumer electronics encased in plastic containing more than one-tenth of 1% of deca-BDE by January 1, 2012, as well as a sales ban on mattresses and upholstered furniture containing the same amount of deca-BDE by January 1, 2008. *See, Brominated Flame Retardants*, Third Annual Report to the Maine Legislature, January 2007.[4] As reported in various media, the Chairperson told state lawmakers in Maine that "there is no question in her mind that deca should be eliminated because it is a persistent toxin that accumulates in the food chain." *See* Kevin Miller, *DEP Urges Legislative Ban on Fire Retardant*, Bangor Daily News, February 16. 2007, at B4.[5] Further, the Chairperson has stated that she would choose an alternative flame retardant over deca-BDE - even if equally toxic - because "[t]he reason we are in this bind is because the industry doesn't have to collect any data about the compounds they are putting into commerce." *Id.*

In addition, the Chairperson has authored two recent articles regarding deca-BDE. The first, entitled *Developmental Delays and Locomotor Activity in the C57BL6/J Mouse Following Neonatal Exposure to the Fully-Brominated PBDE, Decabromodiphenyl Ether* (Neurotoxicology and Teratology, In Press, 2007)[6] suggests that deca-BDE causes adverse effects on the thyroid, however, BFRIP submits there is not reliable evidence to support that theory. Surprisingly, the Chairperson relies on this article in the Final Report to make the same claims regarding effects on the thyroid, but again offers no independent basis upon which to substantiate this claim. *See* Final Report at 24. A second article, called *Risk Assessment and Regulation of PBDEs* (Neurotoxicology and Teratology, 2007)[7], not only appears to promote the ban of deca-BDE, but also apparently relies on the draft RfDs under review in this IRIS assessment which are by no means final nor in a form that should be circulated in the public domain.

While these are just a few examples of public statements made by the external review panel Chairperson relating to deca-BDE, there is no doubt that she has taken a very public position concerning a regulatory determination that is fundamental to the very issues presented to the panelists in the draft IRIS Toxicological Reviews. However, even more disconcerting is the fact that many of these statements and comments concerning deca-BDE were in the public domain *before* the Chairperson was selected for the IRIS External Peer Review. Thus, EPA staff had to know *or should have known* that the Chairperson has been a fervent advocate of banning deca-BDE -- the very sort of policy predisposition that has no place in an independent, objective peer review. *See, e.g.*, Handbook, §3.2.1 at 57 ("[T]he peer review is not for the decision or action itself, but for the underlying scientific and/or technical work product; reviewers should not be asked to provide advice on policy").

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[4] A copy of this report is enclosed as Attachment 1.
[5] A copy of this article is enclosed as Attachment 2.
[6] A copy of the Accepted Manuscript is enclosed as Attachment 3.
[7] A copy of the Accepted Manuscript is enclosed as Attachment 4.

For these reasons, BFRIP believes that the Agency must base its final Toxicological Review on data, opinions, and conclusions other than the Chairperson's. Otherwise, the integrity of this peer review will be further compromised -- which ultimately calls into question the overall integrity of the entire IRIS database.

IV. THE PANEL'S CONCERNS REGARDING THE DATA RELIED UPON IN THE TOXICOLOGICAL REVIEW AND PEER REVIEW

As stated in its formal written comments, BFRIP recognizes that the Agency asserts that a draft Toxicological Review is not yet a final determination made by the Agency.[8] Nevertheless, the documents have been widely circulated and published on EPA's web-pages for purposes of external peer review and public comment and, to the Panel's knowledge, no effort has been made to address the current data deficiencies -- yet these deficiencies are sufficiently profound in certain cases that the draft Review (and any final version containing the same problems) would not meet EPA's own *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated* ("Information Quality Guidelines").

For example, the Review does not comply with the standards for "objectivity" established for data and analyses conducted by federal agencies. "Objectivity" focuses on whether such information "is being presented in an accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate, reliable, and unbiased." Information Quality Guidelines, §5.1, at 15; *see also* 67 Fed. Reg. 8452, 8460 (February 22, 2002). As previously explained, there is real doubt as to whether EPA's apparent willingness to rely on certain studies (especially the so-called "Viberg study") when establishing a reference dose (RfD) for deca-BDE, would meet the Agency's standards for data and information that are both accurate and reliable. At a minimum, BFRIP suggests that the Viberg study is based on a design that does not conform to Agency guidelines for developmental neurotoxicity tests, and that (minimally) the study was not performed in accordance with Good Laboratory Practices ("GLP"). Indeed, some of these same concerns have been raised by the external peer reviewers.[9] *See, e.g.*, Final Report at 12, 13, 15. Furthermore, because (by EPA's own interpretation) the Toxicological Review qualifies as an "influential" scientific risk assessment, the data relied upon (including the Viberg study) must meet certain standards, including:

> (A) The substance of the information is accurate, reliable and unbiased. This involves the use of:

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[8] The Panel reserves its right to file a formal Request for Correction pursuant to the procedures outlined in Section 8 of the Information Quality Guidelines.

[9] It is noteworthy that the complete Viberg study is not believed to be in the possession of EPA, nor was it made available to the external peer reviewers.

> (i) the best available science and supporting studies conducted in accordance with sound and objective scientific practices, including, when available, peer reviewed science and support studies; and
>
> (ii) data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies the use of the data).
>
> (B) The presentation of information on human health, safety, or environmental risks, consistent with the purpose of the information, is comprehensive, informative, and understandable. In a document made available to the public, EPA specifies:
>
> (i) each population addressed by any estimate of applicable human health risk or each risk assessment endpoint, including populations if applicable, addressed by any estimate of applicable ecological risk;
>
> (ii) the expected risk or central estimate of human health risk for the specific populations affected . . .;
>
> (iii) each appropriate upper-bound and lower-bound estimate of risk;
>
> (iv) each significant uncertainty identified in the process of the assessment of risk and studies that would assist in resolving the uncertainty; and
>
> (v) peer-reviewed studies known to the Administrator that support, are directly relevant to, or fail to support any estimate of risk and the methodology used to reconcile inconsistencies in the scientific data.

Information Quality Guidelines, §6.4 at 21-22. As the record stands now, the draft Review fails to meet these requirements established to fulfill the Information Quality Act (and EPA's own Guidelines).

V. THE PANEL'S COMMENTS ON THE FINAL REPORT OF THE EXTERNAL PEER REVIEW

BFRIP has the following specific concerns regarding technical aspects of the External Peer Reviewer's "Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs) Human Health Assessment -- FINAL REPORT" ("Final Report"), dated February 2007 and published on April 4, 2007 (http://cfpub.epa.gov/ncea/cfm/nceawhatnew.cfm).

The Final Report did not demonstrate that the External Reviewers conducted a balanced and reasonable review of the written and oral comments which were provided by BFRIP and other commenters well in advance of the Final Report. For example, BFRIP, ChemRisk, and The Dow Chemical Company each pointed to the critical flaws in the Viberg studies that rendered them too unreliable for IRIS use; instead, one External Reviewer, for example, has stated that there is "no alternative" but to consider Viberg. While it is recognized that one External Reviewer agreed that there were pitfalls with the Viberg studies, and one indicated that "further DNT studies are needed," the overall recommendation of the External Reviewers appears to be that the study was sufficient for IRIS purposes.[10]

This conclusion regarding the Viberg data is completely contrary to the one reached by the Agency when it reviewed similar methods being used by the researcher in EPA's June 2005 VCCEP Data Needs Decision Document ("Decision Document").[11] In the Decision Document, EPA discussed the methods being used in a mouse study by Viberg as it related to some Tier 3 gaps in deca-BDE's neurotoxicity data. It stated:

> EPA notes several issues with the protocol of this study which introduces considerable uncertainty in the interpretation of the results. The issues include the mouse strain, the limited duration of exposure, and the statistical methods. In this study, multiple pups from each litter were tested and this was not controlled for in [sic] the statistical analysis. Similar issues were also raised in the peer consultation meeting. In addition, the European Union recently completed a risk assessment of [deca-BDE] and concluded the results of the Viberg et al (2003) study were not adequate for the purposes of quantitative risk assessment.

Decision Document at 15. Based on these statements, it would seem illogical for the Viberg rat study to be relied upon for the IRIS assessment since the Agency itself previously deemed such methods to be "uncertain" and also reiterated the EU's own determination that the study was "inadequate."[12]

Furthermore, BFRIP continues to disagree that the Viberg data should be used as a basis for IRIS, not only because of their significant limitations in design and transparency of data, and not only because a more robust guideline compliant DNT study is being undertaken, but also due to the fact that non-GLP lab work from one academic investigative lab of Viberg's does not constitute sufficient sound scientific evidence nor has it been shown that his methodologies are a reliable predictor or substitute for the OPPTS/OECD DNT guideline study. Unless or until some independent body has validated that this or other non-traditional type toxicology studies can be substituted for standardized GLP-type studies, they should only be viewed as indicative of a potential hazard, but not used quantitatively to develop RfDs.

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[10] Surely, EPA should hold IRIS to higher standards of data quality.

[11] A copy of the Decision Document is enclosed as Attachment 5.

[12] At another point in the Decision Document, the Agency states that "[t]here is *substantial uncertainty* regarding the interpretation of the behavior effects noted in a recent study [Viberg et al. (2003)] of neonatal mice." Decision Document at 1.

The Final Report also demonstrates that the External Panel did not conduct an independent, balanced, and reasonably thorough review of the extensive science and toxicology database pertinent to deca-BDE, nor the overall weight of scientific evidence relating to PBDEs. For example:

- The available data do not support the conclusion that deca-BDE adversely affects the thyroid, yet the Chairperson's comments suggest that this theory is fact in the Final Report and surprisingly cites her own work from 2007 as support. A more careful review of the article referenced above and enclosed as Attachment 3, indicates that it does not, in fact, demonstrate evidence of an adverse effect.

- Based on current information, there is not adequate basis to conclude (in spite of the position taken by one External Reviewer), that PBDEs are "transgenerational pollutants". Such statements are not based on sound scientific data and represent, at best, speculation and personal opinion rather than careful consideration of the scientific evidence concerning deca-BDE and PBDEs.

- One External Reviewer stated that he is not aware of other peer-reviewed studies that would contribute to an understanding of risks associated with PBDEs. However, an article by Hays and Pyatt, (*Risk Assessment for Children Exposed to Decabromodiphenyl (Oxide) Ether (Deca) in the United States,* Integrated Environmental Assessment and Management, Vol. 2, pp 2-12, 2006) addresses this very issue and should have been identified and made available for consideration by the External Reviewers. Hays and Pyatt conclude in their peer-reviewed article that, based on comprehensive evidence, there are large margins of safety and that the current levels of exposures to deca-BDE are unlikely to represent an adverse health risk.

Furthermore, BFRIP opposes the recommendation of some of the External Reviewers to consider all of the PBDEs as a "group" for IRIS purposes. Such a recommendation lacks insight into the differences among the PBDEs and is contrary to basic scientific and toxicological principles. In fact, one reviewer incorrectly states that PBDEs "have the same toxic end points with varying degrees" and uses this as a rationale to combine the PBDEs into one IRIS document. Another reviewer uses the incorrect and unsupported argument that PBDEs are "additive" for DNT effects with other compounds such as PCBs, in order to rationalize combining the PBDEs into one IRIS document.

Again, it is important to recognize that deca-BDE is a unique and specific substance (structurally, toxicologically, physically, chemically, etc.) and should be evaluated by IRIS independently based on the extensive information already available for deca-BDE. Moreover, the toxicity profile of PBDEs, for example, varies based on the degree of bromination. For the sake of comparison, not even dioxins are considered to be toxicologically equivalent among the various congeners. Thus, there are dioxin TEQs that allow for an independent evaluation of each congener's unique profile. Accordingly, BFRIP urges the Agency not to combine the PBDEs as a group, and to evaluate deca-BDE based on its relevant, substantial, and risk-based database and the comprehensive weight of the evidence.

* * *

In light of the foregoing, the Panel urges you to conclude that these concerns regarding the IRIS PBDE assessment must be addressed before any final reports are published or any republication of the preliminary documents occur. To that end, BFRIP representatives would like to meet with you and the appropriate managers and technical staff responsible for the draft Toxicological Review and the External Peer Review to discuss BFRIP's concerns. We will contact your office soon to set up that discussion. BFRIP looks forward to working with EPA in an effort to resolve these issues in a mutually agreeable manner.

Respectfully submitted,

Sharon H Kneiss

Sharon H. Kneiss
Vice President, Products Divisions
American Chemistry Council

Enclosures

cc: Jim Gulliford, OPPTS
Charlie Auer, OPPT

American Chemistry Council

September 21, 2007

Via Federal Express

George M. Gray, Ph.D.
Assistant Administrator for Research and Development
United States Environmental Protection Agency
Mail Code 8101 R
1201 Constitution Avenue, N.W.
Washington, D.C. 20004

Dear Dr. Gray:

Re: IRIS Peer Review of Polybrominated Diphenyl Ethers (PBDEs)
Docket ID No. EPA-HQ-ORD 2006-0838

This follows up on our previous correspondence on behalf of the American Chemistry Council's Brominated Flame Retardant Industry Panel ("BFRIP" and the Panel")[1] regarding our June 15, 2007 meeting with you and your staff about the ongoing IRIS toxicological reassessment of PBDEs. On the basis of the limited information available on the Agency's IRIS-related web-site pages, it appears that the IRIS reassessment, particularly as it relates to decabromodiphenyl ether ("deca-BDE"), remains in progress. To that end, the Panel submits this letter to address several important concerns.

I. APPARENT REVISION OF THE "FINAL REPORT" OF THE EXTERNAL PEER REVIEW

EPA recently posted a version of the External Peer Reviewer's "Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs) Human Health Assessment – FINAL REPORT" ("Final Report") on its website. The Final Report remains dated February 2007, but appears to have been published on EPA's website on or around August 14, 2007. (http://cfpub.epa.gov/ncea/cfm/nceawhatnew.cfm). The original publication date was April 4, 2007, and that version of the document can no longer be found on the EPA's website. It does not appear that the Agency provided any formal notice that the Final Report was being revised or the reasons for the revision. Indeed, without careful inspection, the reader would not know that the Final Report has been changed or that a previous version had been published. BFRIP requests that the reasons for modifying the Final Report be transparently conveyed on EPA's website.

It appears that the final report was revised in such a manner that all references to and the comments of the peer review panel Chairperson, Dr. Deborah Rice have been removed. BFRIP is pleased that EPA evidently is taking steps to mitigate the appearance of any pre-existing biases against PBDEs, and deca-BDE specifically, that the Chairperson might have articulated in the context of the Peer Review. However, despite the fact that the Chairperson's comments might have been removed from the Final Report, there remain compelling arguments that the entire External Peer Review proceedings may have been inappropriately undertaken.[2]

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[1] BFRIP members are the U.S. manufacturers and importers of brominated flame retardants: Albemarle Corporation, AmeriBrom, Inc., and Chemtura Corporation.

Consequently, BFRIP remains interested in hearing from you concerning the ways in which the Agency intends to ensure that the Chairperson did not inappropriately influence (even if unintentionally) the views of other Peer Review Panelists or otherwise have a direct impact on the overall outcome of the Panelists' conclusions. Thus, unless there will be greater transparency and substance to the measure being taken by EPA to correct this awkward situation, BFRIP is likely to remain of the position that the *entire* peer review process has been compromised.

II. CONTINUED CONCERNS REGARDING THE DATA BEING RELIED UPON IN THE TOXICOLOGICAL REVIEW AND PEER REVIEW PROCESS

As stated in its formal written comments, previous correspondence, and during our June 15 meeting with EPA, BFRIP continues to have serious concerns regarding the data relied on by the Agency in the draft Toxicological Review for deca-BDE.[3] Furthermore, the Panel's concerns were not resolved by the revisions made to the Final Report, since only certain comments were eliminated, and the document fundamentally remains the same. *

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CPR!

One of BFRIP's chief concerns is that the complete Viberg study (including supporting data) is not in the possession of EPA, nor was it made available to the external peer reviewers. We understand that EPA took steps to obtain the individual animal data from Viberg et al.[4,5] Though the study authors refused to provide the data, EPA failed to notify the general public that EPA's data request was denied. Moreover, this information should have been transparently conveyed in the external charge questions. It was not.

There is considerable doubt as to whether EPA's reliance on the Viberg study when establishing a reference dose (RfD) for deca-BDE, would meet the Agency's own standards for data and information that are both accurate and reliable. There is no doubt that the Viberg study is based on a design that does not conform to Agency guidelines for developmental neurotoxicity tests, and there is no basis in the record to conclude that the study was performed in accordance with Good Laboratory Practices ("GLP"). The results of the study thus must be viewed in a limited context.

BFRIP continues to disagree with EPA that the Viberg data should be considered during the IRIS reassessment because: a) there are significant limitations in study design and transparency; b) a more robust guideline compliant DNT study is being undertaken; and c) non-

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[2] One must continue to question how the Agency's procedures allowed the issue to be overlooked until raised by BFRIP in prior correspondence.

[3] BFRIP recognizes that the Agency asserts that a draft Toxicological Review is not yet a final determination and, therefore, not subject to challenge under EPA guidelines. *See Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated.* Accordingly, the Panel must reserve its right to file a formal Request for Correction pursuant to the procedures outlined in Section 8 of the Guidelines should the Review (and the resulting reassessment) still contain deficiencies once it is officially completed and published.

[4] Freedom of Information Act Request HQ-RIN-01639-07 (hereinafter FOIA) (Request for "a copy of e-mails, facsimiles, memorandums, meeting notes, phone call records, etc containing information on the U.S. Environmental Protection Agency's (EPA) data request from Viberg et al. [Henrick Viberg, Anders Frederiksson, and Pers Eriksson (Uppsala University); Eva Jakobsson and Ulrika Orn (Stockholm University)]".

[5] Electronic communication From: Joyce Donohue, To: Per Eriksson and Henrik Viberg, Subject: Request for Assistance – U.S. EPA Office of Water, (Sent 02/02/2005 11:04 AM) (Request for "a more extensive set of the individual animal data than that found in the published reports.")

GLP lab work from one academic investigative lab (such as the Viberg study) does not constitute sound scientific evidence in this context. Unless and until the underlying data and a full report are published and an independent body has validated that the Viberg or other non-traditional type toxicology studies can be substituted for standardized GLP-type studies, such studies only should be viewed as indicative of a *potential* hazard, but not used quantitatively to develop RfDs.

III. REQUEST THAT EPA PROVIDE UPDATED INFORMATION ON THE STATUS OF THE IRIS REASSESSMENT

BFRIP remains concerned about the IRIS reassessment and continues to find that the materials posted on EPA's websites do not reflect the current status of the process. Accordingly, the Panel respectfully requests that the Agency provide an update to us on the progress of the IRIS reassessment (including a revised timeline for when certain milestones are estimated to be met), and information concerning the Agency's intentions with regard to correcting any underlying bias on the part of the Peer Review Panelists and their Chairperson.

The Panel appreciates your time and the energy you have devoted to listening to and addressing our significant concerns. We look forward to receiving EPA's response to this letter. We would be happy to meet with you again to further discuss these issues. Please feel free to call me at **703-741-5605** or email me at **nancy_sandrof@americanchemistry.com** should you have any questions.

Respectfully submitted,

Nancy Sandrof

Nancy Sandrof, M.P.H.
Manager, BFRIP
American Chemistry Council

cc: Jim Gulliford, OPPTS
Charlie Auer, OPPT

publication we provided during our meeting, entitled, "Statistical issues and techniques appropriate for developmental neurotoxicity testing".[2] The authors of this EPA co-sponsored study summarized the methodology used by Viberg *et al.* by stating "[t]his conclusion is inaccurate", "[t]here are litter effects on spontaneous motor activity", and "[i]gnoring litter effects in the statistical analysis of DNT studies is simply not an acceptable practice".[3] The unwillingness of the Viberg study researchers to provide the individual animal data to EPA, and the Agency's omission of this information in the Toxicological Review of Decabromodiphenyl Ether and the External Peer Review Charge, continues to make it impossible for EPA's selected Peer Reviewers and others to perform any independent data analysis as would be expected in a scientific review.

EPA's general assessment factors for evaluating data quality and relevance at a minimum require a discussion of "[t]he extent of independent verification, validation and peer review of the information or of the procedures, measures, methods or models."[4] EPA's failure to include the following information is a clear violation of this guidance for these reasons: 1) the Viberg group were unwilling to share their individual animal data;[5,6,7] 2) Viberg *et al.* (2003), were unable to identify which pups came from which litters;[8] 3) the Viberg 'model' contradicts EPA's own guidance,[9,10] as well as, the OECD

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[2] Holson *et al.* (2007). *Statistical issues and techniques appropriate for developmental neurotoxicity testing. A report from the ILSI Risk Science Institute Expert Panel on neurodevelopmental endpoints.* NEUROTOXICOLOGY AND TERATOLOGY, Vol. __, doi: 10.1016/j.ntt.2007.06/001, pp. 1-23.

[3] *Id.* at p. 10.

[4] EPA (2003) *A summary of general assessment factors for evaluating the quality of scientific and technical information*, EPA 100/B-03/001, pp. 1-11, at p. 8.

[5] Freedom of Information Act Request HQ-RIN-01639-07 (hereinafter FOIA) (Request for "a copy of e-mails, facsimiles, memorandums, meeting notes, phone call records, etc. containing information on the U.S. Environmental Protection Agency's (EPA) data request from Viberg *et al.* [Henrick Viberg, Anders Frederiksson, and Per Eriksson (Uppsala University); Eva Jakobsson and Ulrika Orn (Stockholm University)]".

[6] Electronic communication From: Joyce Donohue, To: Per Eriksson and Henrik Viberg, Subject: Request for Assistance – U.S. EPA Office of Water, (Sent 02/02/2005 11:04 AM) (Request for "a more extensive set of the individual animal data than that found in the published reports.")

[7] Peter W. Preuss, (FOIA response letter dated August 15, 2007)(EPA was unable to obtain data from Per Eriksson and Henrik Viberg, despite the requests from Joyce Donoghue at the EPA's Office of Water).

[8] VCCEP (2003) *Report of the Peer Consultation Meeting on Decabromodiphenyl Ether*, Submission by American Chemistry Council's Brominated Flame Retardant Industry Panel for the Voluntary Children's Chemical Evaluation Program, Peer Consultation Organized by Toxicology Excellence for Risk Assessment, pp. 1 – 101, at p. 11 <http://www.tera.org/peer/VCCEP/DECA/VCCEP%20DBDPO.pdf>

[9] EPA (1998) *Health Effects Test Guidelines OPPTS 870.6300 Developmental Neurotoxicity Study*, pp. 1 – 12

[10] EPA (2000) *Benchmark dose technical guidance document*, EPA/630/R-00/001, pp. 1 – 87, at p. 73 "In general, data from developmental toxicity studies in rodents are best modeled using nested models. These

Developmental Neurotoxicity Study guidance;[11] and 4) an EPA co-sponsored study published with an EPA co-author found the Viberg 'model' unacceptable. In light of these issues, which we have explained in greater detail in our submissions, reliance on the Viberg study to establish an RfD cannot be justified, and doing so would contradict well-established, published OMB and EPA data quality guidelines and the "Data Quality Act". If ORD staffs are considering additional data, *e.g.*, Viberg *et al.* (2007),[12] in their decision-making process, we encourage them to reconsider, as this EPA/Viberg collaboration suffers from the same fundamental flaws as those found in Viberg *et al.* (2003).

As we indicated, BFRIP has provided EPA with a study protocol for review from the DNT Study being sponsored by the Panel members. We will continue to make interim study data available to the Agency throughout the progress of the study as well as the draft study report which is expected to be available in late 2008. We appreciate your review of the information we have provided and request that EPA address the issues outlined herein, and in our previous submittals, before issuing its IRIS Reassessment of DecaBDE.

If you have any questions or new developments on the IRIS Reassessment of DecaBDE, please contact me at 703-741-5605 or nancy_sandrof@americanchemistry.com

Sincerely,

Nancy Sandrof

Nancy Sandrof
BFRIP Panel Manager

cc: BFRIP

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models account for any intralitter correlation, or the tendency of littermates to respond similarly to one another relative to the other litters in a dose group."

[11] OECD (2007) *Developmental Neurotoxicity Study*, OECD GUIDELINE FOR THE TESTING OF CHEMICALS #426, pp. 1 – 26, "[t]he statistical unit of measure should be the litter (or dam) and not the pup." at p. 4.

[12] Viberg *et al.* (2007) Neonatal exposure to decabrominated diphenyl ether (PBDE 209) results in changes in BDNF, CaMKII and GAP-43, biochemical substrates of neuronal survival, growth, and synaptogenesis, NEUROTOXICOLOGY, Vol. __, doi: 10.1016/j.neuro.2007.10.007, pp. 1-26.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN - 8 2007

OFFICE OF
RESEARCH AND DEVELOPMENT

Nancy Sandrof, M.P.H.
Manager, BFRIP
American Chemistry Council
1300 Wilson Boulevard
Arlington, Virginia 22209

Dear Ms. Sandrof:

Thank you for your letter of September 21, 2007, providing further comments on behalf of the American Chemistry Council's Brominated Flame Retardant Industry Panel (BFRIP) regarding the external peer review of the draft health assessments for the polybrominated diphenyl ethers (PBDEs). As mentioned, your letter follows up on our June 15, 2007, meeting during which EPA acknowledged your concerns and indicated that we would take actions to respond to some of these concerns. Following the outline laid out in your letter, I am pleased to have this opportunity to reply to your comments and answer your questions.

I. REVISION OF THE EXTERNAL PEER REVIEW REPORT

Your September 21 letter requested that the reason for the modification of the external peer review Final Report be conveyed on EPA's Web site. At the June 15 meeting, EPA listened to your concerns about a potential conflict of interest on the part of the Chairperson for the IRIS external peer review of the draft PBDEs Toxicological Reviews. At that time, we said we would consider your concerns and possibly make changes to the report. Since then, we have decided that the Chairperson's comments would not be considered in the EPA's response to the external peer reviewers and that the Chairperson's comments would be removed from the Final Report of the external peer review. Both of these actions have been taken. Further, EPA added a statement to the Integrated Risk Information System external peer review web site that indicates the change in the report is due to our determination that one of the panel members had a potential conflict of interest.

In addition, you requested more information concerning the ways in which the Agency intends to ensure that the Chairperson did not influence the views of the other PBDE peer review panelists. To evaluate the Chairperson's potential influence on the other peer review panelists, the initial and final comments received from all of the external peer reviewers were comprehensively reviewed by EPA. This review revealed minor additions to the Final Report following the discussions during the public meeting and provided no evidence that the Chairperson significantly influenced the other panelists.

II. QUALITY AND USE OF THE VIBERG ET AL. STUDIES

You also indicated concern about the quality of the Viberg et al. study, which was published in the peer reviewed literature, and the availability of the underlying data. In the draft Toxicological Reviews for the PBDEs, the Agency included a detailed summary of the Viberg et al. study design and methods. The selection of the principal study was included as a charge question during the external peer review of the PBDE IRIS assessments. The external peer reviewers acknowledged the limitations and concerns with the study. However, all of the reviewers agreed that the studies from the Eriksson/Viberg laboratory were appropriate for derivation of the RfDs for the PBDE congeners and that the studies' limitations were transparently discussed in the Toxicological Reviews. The neurobehavioral effects reported by the Eriksson/Viberg group are supported by multiple studies performed within this group and an expanding body of literature on PBDEs.[1] Additionally, the results from a study recently completed, but not yet published, by the U.S. EPA National Health and Environmental Effects Research Laboratory[2] details changes in motor and cognitive activity in rodents following administration of single or repeated perinatal doses of PBDEs, which are similar to the effects reported by Eriksson and Viberg.

III. TIMELINE/IRIS TRACK

Finally, you requested an update on progress of the IRIS reassessment, including a revised timeline. The completion dates for four PBDE IRIS assessments were changed to provide adequate time to address final interagency review comments. The IRIS Track will be updated weekly or more often to reflect the current estimated completion dates.

Again, thank you for your letter and your continued interest in EPA's IRIS assessment of the PBDEs. Should you have any questions, please contact me or you may contact Dr. John Vandenberg, Associate Director for Health, National Center for Environmental Assessment in the Office of Research and Development. Dr. Vandenberg may be reach at 919-541-4527 or by email at ***vandenberg.john@epa.gov.***

Best regards,

George Gray

George Gray

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[1] Branchi et al., 2002; Kuriyama et al., 2005; Rice et al., 2007.

[2] Electronic mail from Ginger Moser, National Health and Environmental Effects Research Laboratory, Research Triangle Park, North Carolina, to Samantha Jones, U.S. EPA, dated August 14, 2007

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WASHINGTON, D.C. 20460

JAN - 8 2007

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Best regards,

George Gray

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[1] Branchi et al., 2002; Kuriyama et al., 2005; Rice et al., 2007.

[2] Electronic mail from Ginger Moser, National Health and Environmental Effects Research Laboratory, Research Triangle Park, North Carolina, to Samantha Jones, U.S. EPA, dated August 14, 2007

STATE OF MAINE
OFFICE OF THE GOVERNOR
1 STATE HOUSE STATION
AUGUSTA, MAINE
04333-0001

JOHN ELIAS BALDACCI
GOVERNOR

March 17, 2008

The Honorable Stephen Johnson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Dear Administrator Johnson:

I was very disappointed to learn that at the request of a chemical industry lobbyist, your agency dismissed the chairperson of the External Review Panel developing a key health standard for Deca PBDE and other brominated fire retardants that contaminate human blood and breast milk.

The chairperson, Dr. Deborah Rice, is an award-winning, retired EPA scientist now with the Maine Center for Disease Control and Prevention. Dr. Rice is also an Associate Editor of the peer-reviewed journal Neurotoxicology. According to the chemical industry, Dr. Rice displayed an "appearance of bias" by stating the position of the Maine Department of Health and Human Services in support of state legislation to restrict Deca in a scientific briefing and work session presentation before the Natural Resources Committee of the Maine Legislature. In response, your agency removed Dr. Rice from the panel, stripped her comments from the final panel report, and republished the altered document.

In their request for Rice's removal, the chemical industry lobby group, the American Chemistry Council cited EPA guidance that cautions against selecting expert reviewers with an "appearance of lack of impartiality." But the guidance also counsels EPA to avoid choosing reviewers for whom the matter at hand has "a direct and predictable effect on [their] financial interest" or when "circumstances would cause a reasonable person with knowledge of the relevant facts to question his impartiality in the matter" (EPA 2006). Removal of Dr. Rice from the panel appears contrary to this guidance.

This action by your agency creates a questionable framework in which state or federal scientists who represent the views of their agencies in public, or any expert who concludes based on their review of the peer-reviewed science that a chemical may present a risk to the public health, will be barred from EPA expert panels. Given the value of and public trust in state and federal scientists who base their conclusions on peer-reviewed science, this runs counter to the best interests of the public health.

To rebuild public trust in the independence of the Agency's science and decision making, I respectfully request that you reinstate Dr. Rice as chair of the Deca panel and restore her comments to the expert panel report.

PRINTED ON RECYCLED PAPER

PHONE: (207) 287-3531 (Voice)
888-577-6690 (TTY)
www.maine.gov
FAX: (207) 287-1034

I look forward to receiving your reply.

Sincerely,

John E. Baldacci
Governor

cc: Senator Olympia Snowe
Senator Susan Collins
Congressman Tom Allen
Congressman Michael Michaud

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 10 2008

DEPUTY ADMINISTRATOR

Mr. Bill Roderick
Deputy Inspector General
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Dear Mr. Roderick:

I am requesting the Inspector General's Office investigate a matter involving Dr. Deborah C. Rice.

It has been brought to my attention (see attached letter) that last year Dr. Rice was one of a number of scientists on an expert panel that was used to peer review an Environmental Protection Agency Integrated Risk Information System assessment regarding the chemical deca-BDE. Deca-BDE is a polybrominated diphenyl ether used as a fire retardant that may also pose risks to public health. According to the attached letter, Dr. Rice was recently removed from this panel.

I would like the Inspector General to:

1. determine whether the removal of Dr. Rice and any actions taken by EPA or Dr. Rice directly related to her removal from this panel were done consistent with existing federal law, regulations, guidance and other relevant requirements;
2. whether the current laws, regulations, guidance and other relevant requirements for such panels are adequate to produce objective scientific reviews; and
3. make recommendations as to how the current system of populating and managing such expert panels could be improved.

Thank you for your assistance regarding this matter.

Sincerely,

Marcus Peacock

Attachment

Internet Address (URL) • http://www.epa.gov
Recycled/Recyclable • Printed with Vegetable Oil Based Inks on 100% Postconsumer, Process Chlorine Free Recycled Paper

External Peer Review

Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs) Human Health Assessment

FINAL REPORT

Prepared for
Integrated Risk Information System (IRIS) Program
Office of Research and Development
National Center for Environmental Assessment
U.S. Environmental Protection Agency

Prepared by
ORISE IRIS Technical Assistance Team
Oak Ridge Institute for Science and Education
Oak Ridge Associated Universities

February 2007

This document was prepared for the EPA by ORISE under Interagency Agreement
No. DW-89939822-01-0 between EPA and the U.S. Department of Energy.
ORISE is managed by Oak Ridge Associated Universities under a contract with DOE.

Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs)

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EXTERNAL PEER REVIEWERS

Deborah Rice, Ph.D., Chair
State of Maine

Ahmed E. Ahmed, Ph.D.
University of Texas Medical Branch

Richard J. Bull, Ph.D.
MoBull Consulting

Lucio G. Costa, Ph.D.
University of Washington

Ralph Kodell, Ph.D.
University of Arkansas for Medical Sciences

The ORISE IRIS Technical Assistance Team has neither altered nor edited these comments for grammatical or other errors.

Peer Review Project

Samantha Jones, Project Manager
U.S. Environmental Protection Agency

Leslie Shapard, Senior Peer Review Manager
Oak Ridge Institute for Science and Education

The U.S. EPA's National Center for Environmental Assessment (NCEA) has developed several draft Toxicological Reviews for Polybrominated diphenyl ethers. Specifically, toxicological review documents have been developed for tetra-, penta-, hexa-, and decabrominated diphenyl ethers. The charge questions below specifically address the polybrominated diphenyl ethers assessment.

GENERAL QUESTION

Are you aware of other published peer-reviewed toxicological studies not included in these Toxicological Reviews that could be of relevance to the health assessment of BDE-47, BDE-99, BDE-153 or BDE-209?

Deborah Rice, Ph.D., Chair

The Agency does not discuss or justify separating the PBDE congeners and deriving separate RfDs for only four of them, nor does it discuss how the congeners were chosen. (However, if only four congeners were to be choses, the ones chosen are the best ones: 47 and 99 are historically the most prevalent in human tissue, 153 is increasing and is the most prevalent in some recent samples, and 209 is still sold in the U.S. and may be degraded and metabolized to other congeners.) There is no acknowledgement in these documents that these congeners will be additive for at least some endpoints, including developmental neurotoxicity. There is also no recognition that PBDEs will probably be additive with PCBs, and perhaps other chemicals as well, such as methylmercury. There are mechanistic data supporting the notion that PCBs and PBDEs act by the same mechanism for neurotoxicity, for example. EPA typically considers such information in the choice of UFs.

The four documents should be combined into one. There is a lot of repetition that makes the whole package much longer than it needs to be. More importantly, the richness and consistency of the database is not apparent in the current organization. Studies from other congeners and mixtures should also be included. There are data on MOA that are appropriate to include, and are more relevant than what is in the current documents. The documents do not adequately present the potential for metabolism of these congeners to lower-brominated compounds that are also toxic. This is especially relevant for 209, which is metabolized (and degraded in the environment) to toxic congeners. Since an RfD is supposed to represent a lifetime daily intake, which would result in metabolism and accumulation in the body over the course of a lifetime, this must be incorporated into the RfD derivation.

The criteria by which papers were eligible for inclusion in these documents is unstated and unclear. The documents contain reference to an abstract of a presentation at the Society of Toxicology meeting. The conclusions from that abstract are critical to the suitability of the choice of critical studies, since it provides reassurance that the treatment of littermates as independent observations by the Swedish group does not render the conclusions from those studies uninterpretable. Similarly, a thesis is the main reference provided for the assertion that PND10 represents a unique critical period in mouse development, which argument is pivotal to the choice of uncertainty factors. Unpublished studies from industry are also included. Given that, it would be appropriate and informative to include the four-page extended abstracts from the Dioxin meeting, at least for the last couple of years. For example, the 2006 meeting included a report of associations between a number of congeners and human health effects. Papers were also presented reporting interactions between BDE-99 and methylmercury and BDE-209 and PFOA to produce neurotoxicity. BDE-99 also interacts with PCBs (Eriksson *et al.*, Toxicol. Sci., in press). Other groups have also performed analyses of PBDEs in human tissue, and there is no reason to exclude these data. Perhaps non-peer-reviewed references could be marked with an asterisk.

The documents should also include metabolic studies in wildlife, for example Heather Stapleton's work in fish. These documents also do not accurately reflect the change in congener pattern in humans and in animals over time, suggesting metabolism of more highly-brominated congeners to lower-brominated congeners, that has been observed in animals (e.g. the finding of higher levels of 153 than 99 in breast milk or blood in the U.S.: EWG, 2003 and Schecter *et al.*, 2005). (Additionally, the Swedish group make the argument that it is probably metabolites and not the parent compound that produced toxicity in mice and rats after administration of 209, and yet with the extensive description of this study, this is not mentioned.) This failure does not provide a complete picture of the potential for these congeners to produce toxicity via metabolism to other toxic metabolites following chronic (lifetime) exposure.

Ahmed Ahmed, Ph.D.

I have examined the available literature, for the past 10 years, for BDE-47, BDE-99, BDE-153, and BDE-209 by searching under their individual chemical name and chemical abstracts number (CASRN) and crossing the outcome with adverse effects, cancer and/or systemic or genetic toxicity,. I found about 200 citations and their abstracts which represent various types of studies on these compounds. The majority, if not all, of these references are included in various "Toxicological Review" document for one or the other of these chemicals. A detailed literature search analysis is included in this report. The authors of the document may need to verify the existence and use of the appropriate citations in the reviews using the reference manager software programs.

The Toxicological reviews for BDE-47, BDE-99, BDE-153, and BDE-209 are extremely detailed and commonly repetitive. The same information is repeated several times in the same document under different headings (subsection) and in documents for other congeners. Although these repetitions are distracting, I realize they are pluses rather than negatives, I believe that was done to emphasize particular point or effect, to establish the validity of a study and its results and to point out the drawbacks in experimental design or data analysis and interpretation. Therefore, I find the quality of these review documents in a "good to excellent" range. In some of these reviews however, the lack of scientific information makes the decision making processes difficult due to limited number of studies or narrow scientific objectives that disregarded other possible interpretations. This problem does not point to any shortcomings in the efforts of the authors of these documents. Rather it indicates the limitation and shortage of available information (studies).

In a general sense, these chemicals are congeners of each other and because each one is contaminated by one or more of the others. Also, they metabolically, under environmental and biological conditions, are inter-convertible to each other (compounds with higher bromine numbers are converted to compounds with lower bromine). Therefore, I believe that putting them all in one comprehensive review document would serve the purpose more adequately. They almost have the same toxic end points with varying degrees. The effects of these compounds, which came from limited number of studies, are repeatedly compared in each document for each individual compound.

Metabolic and distribution studies are extensively described in the document without deep scientific interpretation of the results nor how these results could be interpreted in the evaluation of human body burden. Furthermore, the purities of the radioactive chemicals used in most studies were not cited. The position of the label as well as the specific activities of the 14C compounds, used in these studies were not indicated in most sections. I am also troubled by the different ways used for the presentation of the doses and concentrations of the compounds and their metabolites in biological tissues (umole, ug, percent of the dose). A unified parameter should be used to insure comparative analysis and easy follow up.

Richard Bull, Ph.D.

I am not aware of other peer-reviewed toxicological studies that would contribute to an understanding of risks associated with these PBDE's. However, some papers included in the review should be better integrated into the derivation of the reference doses.

Lucio Costa, Ph.D.

There are a number of publications that have not been included in the Reviews and that may be relevant to the health assessment of BDEs.
A few studies indicated that house dust is a major source of exposure to BDEs, and for toddlers in particular, dust has been estimated to account for 80% of BDE exposure.

- Jones-Ortazo HA et al., Environ. Sci. Technol. 39: 5121-5130, 2005
- Wilford BH et al., Environ. Sci. Technol. 39: 7027-7035, 2005
- Schecter A et al., J. Toxicol. Environ. Health Part A 68: 501-513, 2005

Contamination of food with BDEs has not been mentioned, yet diet is believed to contribute to the overall body burden of BDEs.

- Hites RA et al., Environ. Sci. Technol. 38: 4945-4949, 2004
- Schecter A et al., Environ. Health Perspect. 114: 1515-1520, 2006

High levels of BDEs were found in children (case study).

- Fischer D et al., Environ. Health Perspect. 114: 1581-1584, 2006

Levels of BDEs were recently determined in plasma of pregnant women in California.

- Bradman A et al., Environ. Health Perspect. 115: 71-74, 2007

~~Various studies have explored possible mechanisms of action of BDEs, including activation of~~ protein kinase C and induction of oxidative stress.

- Kodavanti PRS, Derr-Yellin EC, Toxicol. Sci. 68: 451-457, 2002
- Kodavanti PRS et al., Toxicol. Sci. 88: 181-192, 2005
- Reistad T, Mariussen E, Toxicol. Sci. 87: 57-65, 2005
- Reistad T et al., Arch. Toxicol. 80 : 785-796, 2006

Ralph Kodell, Ph.D.

I am not aware of any other relevant studies.

1. QUESTIONS RELATED TO THE DERIVATION OF THE REFERENCE DOSE

FOR BDE-47, BDE-99, BDE-153 and BDE-209

1.1 Have the rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies been transparently and objectively described in the draft Toxicological Reviews of BDE-47, BDE-99, BDE-153 and BDE-209? Are there additional studies that should be considered for deriving the RfDs for any of the four PBDE congeners?

Deborah Rice, Ph.D., Chair

The use of an abstract to partially justify use of the Swedish studies is unacceptable. EPA must provide summary statistics, including measures of variance, comparing protocols using littermates as independent observations vs. using a single pup/litter. The SOT abstract just states that results under the two protocols are significant, which is not adequate. The legitimacy of the choice of these studies is dependent upon this information. In addition, the MOA of there observations is unknown and is probably not the result of perturbation of the cholinergic system. The documents need to be revised with respect to what is known about MOA (nothing). This has implications for the repeated assertions about PND 10 being a super-sensitive period of development for these endpoints, let along the universe of behavioral, neurochemical, and neurophysiological endpoints that have not been assessed.

Ahmed Ahmed, Ph.D.

In all the documents provided, except for BDE-209, no cancer related data was available. In each individual document for every compound there were several sporadic, non cancer related, referenced molecular and systemic toxicological studies. Most of the available and presented studies, unfortunately, toxicological and molecular (receptor binding etc.), were designed to look for the effect(s) of these modern environmental pollutants in light of the toxicological effects of traditional and well studied compounds such as PCB. The large numbers of the reported molecular studies on BDEs were tailored after the effect of poly chlorinated aromatic hydrocarbons. Although the chemicals under review (BDE) are halogenated (brominated) aromatic hydrocarbons, these tailored studies back fired. That is because we ended up with a number of negative or nonspecific effects and obtained limited information to use for the proper evaluation of the risk from BDEs.

The few available systemic toxicological studies are blemished by the fact that most of these studies came from the same laboratory. Although, the data seems to be academically solid, their validity and strength is debatable because it has not been verified in various other laboratories neither in the U.S. nor in other countries. This factor alone weakens but not hinders the derivation of the specific RFD. It makes the confidence in these RFD's low

The authors of the Toxicological Reviews for BDE-47, BDE-99, BDE-153, and BDE-209 have to base their derivation of RFD on continuous scientific information. They used those studies that have specific doses and defined time of exposure as well as a defined adverse effect(s). The only available studies that have dose response and time course were those described by the authors in the texts and were used for the derivation of RFDs. With this in mind, they have clearly and very transparently derived the rational for using these studies. They also took into consideration all drawbacks that weakness each particular study. I was impressed by the way they listed at least 6-10 points explaining their concerns for the use of particular data, in each selected study, in the derivation of RFD for each individual compound. Meanwhile they documented the rational for using the study in their derivation of RFD. There was very clear presentation of the pros and cons of each study utilized in the estimation of RFD.

Richard Bull, Ph.D.

The data available on most of these compounds is quite limited (BDE-209 being somewhat of an exception). In most cases, the risk assessment focuses solely on results from a non-conventional neurodevelopmental test. In one case, BDE-209, a conventional reproductive/developmental toxicity test found no effects at doses much higher than observed in the neurobehavioral study. This may reflect the insensitivity of conventional reproductive/developmental toxicity tests OR more likely, increasingly smaller fractions of the doses being absorbed as doses are increased. The doses utilized were huge, 100, 300 and 1000 mg/kg in corn oil. One would predict that the aqueous phase through which these compounds would have to diffuse to get to an absorptive surface to be exceeded at doses orders of magnitude lower than the lowest dose! Nevertheless, the discrepancies raise significant issues with the standard application of uncertainty factors to results that are clearly more sensitive than conventional methodologies. To put this starkly, either the UFs applied to the "standard" test data are way too small OR smaller UFs need to be applied to these data must be adjusted to account for their much greater sensitivity (and specificity).

There are particular UFs that appear completely inappropriate in the current derivation of reference doses. For example, defaulting to a database uncertainty factor when data of this relative sensitivity to conventional evaluations of reproductive/developmental results are available is very inappropriate.

A more central role also needs to be given to the neurochemical data that is provided, especially those that utilized essentially parallel study designs to the neurobehavioral studies. They are presented as supporting data. They are a lot more than that. They provide an organic measure of modified neural development. It may not be entirely clear how the neurobehavioral and neurochemical data are linked functionally, nevertheless, the two data types contribute as an independent measures that there is an apparently permanent alteration in development. This type of corroborating data should be taken as being much more critical than data from 'standard protocols'. Targeted data of this kind in developmental neurotoxicity would be useful if broadly available. It is simply too expensive and time consuming to identify "critical" endpoints for every compound subjected to safety assessments when the expectation is that such effects are relatively rare. The neurobehavioral data may still be the most appropriate to use for the dose-response assessment, but in a sense the neurochemical data are the critical information. Until I found that data in the documents, I was teetering to the point of saying neurobehavioral data was an inappropriate, unsupported, and poorly understood endpoint (despite what is said in the guidelines).

The more critical question with the apparent developmental impacts of the PBDEs is the apparent consistent developmental neurotoxicity that is seen within this class of compounds. This is observed despite very different patterns of metabolism, distribution, and persistence of these compounds in the body. Some effort should have been expended to see if the relative potency of the PBDEs could be rationalized considering the differences in the extent of metabolism.

On the other hand, one has to be concerned that very similar data have been generated by this same laboratory on a broader set of unrelated compounds. It is time to be concerned about the specificity of these data for developmental neurotoxicity. Independent confirmation is essential when such a apparently non-specific endpoint ends up flagging everything studied.

I most strenuously object to the treatment of these single-dose experiments as being equivalent to a subchronic exposure when applying uncertainty factors to arrive at an RfD. This is justified on the basis that brain development does not occur at an equivalent rate over a lifetime. This question is very relevant to whether of not a body burden approach should have been taken for this endpoint. Scientifically, the question is whether a body burden accumulated over time before the critical period would have the same impact as tissue levels that were achieved by the single dose protocol that was used. The available data do not allow this possibility to be evaluated. Therefore, the assumption that the acute dose at PND 10 is equivalent to a subchronic exposure is highly suspect.

Obviously, the data that are available are not sufficiently developed to allow the development of PK models. However, if evaluated critically (i.e. all the data are not equally informative as indicated in the editorial comments appended to the response to the formal questions) there may be enough absorption, distribution, and elimination data to make some ballpark estimates of consistent measures of how much of the parent compound and/or metabolites are present in tissues. The essential question is whether the effects of 1/10 the dose administered between PND 0 and PND 10 are the same as the full dose that is administered that is administered on PND 10. This experiment or an analogous one has not been done. Therefore, no conclusions can be made. Until such data are available, these studies have to be treated as a single dose studies, not a subchronic exposure.

There is some serious question related to whether the anti-thyroid effects of these compounds are of importance to the neurodevelopmental effects observed. The data of Zhou et al. (2002) establishes that the antithyroid effects are observed with DE-71, a formulation that might be reasonably linked to neurodevelopmental effects observed with BDE-47 and BDE-99. The Zhou et al. (2002) study was very well done and included not only good dose-response information, but a probable mechanism for the observed effects on thyroid hormone(induced metabolism of thyroid hormone metabolism). As pointed out in more detail in the editorial comments below, the thyroid effects seen in this study occur at doses that are higher than those that produce the neurodevelopmental effects of BDE-47 and BDE-99. As a result, the conclusion needs to be made that the neurodevelopmental effects cannot be linked to the anti-thyroid effects of these compounds.

Lucio Costa, Ph.D.

The rationale and justification for deriving RfDs on the basis of neurobehavioral toxicity studies have been well described and documented. The additional studies indicated above, particularly on body burden in infants and toddlers, would strengthen the health assessments, though they will not change the final determination of RfDs.

Ralph Kodell, Ph.D.

Limited human data do not indicate an association between exposure to PBDEs and adverse health outcomes. However, these data are insufficient to conclude that there is no potential for such effects. For BDE-47, BDE-99 and BDE-153, neurobehavioral effects are the only toxic effects that have been observed consistently in rodent studies of PBDEs, and therefore provide the only data for deriving RfDs. For BDE-209, the NTP rat and mouse bioassays (NTP, 1986) provide suitable data on noncancer endpoints other than neurobehavioral endpoints. The rationale for basing the RfD for BDE-209 on neurobehavioral effects instead of the other effects is that the neurobehavioral effects lead to the lowest point of departure. The rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies is transparent and appears to be objective. I do not know of additional studies that should be considered for any of the PBDEs. However, among the studies that have been considered, I think that greater consideration should be given to some of the studies other than the Eriksson/Viberg studies. Specifically, the studies of Branchi et al. (2002) and Kuriyama et al. (2005) provide data on BDE-99 that is suitable for deriving an RfD. The Branchi data have not been modeled while the Kuriyama data have been modeled but not used.

As noted in the documents, an association between neonatal exposures to BDE-47, BDE-99, BDE-153 or BDE-209 and neurobehavioral dysfunction in humans has not been established. Nevertheless, the behavioral studies appear to provide the most appropriate, dose-response data on adverse noncarcinogenic effects on which to base the health assessment of the four PBDE congeners.

1.2 Do you agree or disagree with EPA basing the health assessment of BDE-47, BDE-99, BDE-153 and BDE-209 to a large extent on the Eriksson/Viberg neurobehavioral studies?

Deborah Rice, Ph.D., Chair

The meaning of this question is unclear. I agree with the choice of the Swedish studies for the RfD derivation for 3 congeners, but not the fourth (see below). However, I do not agree with the choice of the habituation ratio as the endpoint. This is a non-standard derived measure, and its significance is not clear. The results may or may not represent failure to habituate. If the Swedish investigators think that this is the behavioral mechanism for their findings, they should have directly tested habituation with a number of additional tests. The actual data for the various endpoints should be used instead. (This is probably an answer to 1.4, but all these questions run together and in many ways are the same question.)

Ahmed Ahmed, Ph.D.

As described earlier, the limitation of the availability of complete and comprehensive one or more studies that evaluate various types of adverse effects of these chemicals necessitated the utilization of what is available such as Eriksson & Virberg neurobehavioral studies. It is well known that there could be no one complete and comprehensive toxicological study. Every individual study will have its own limitation. In spite of some technical weaknesses in these studies, there use in the risk and RFD estimation is warranted.

The reason for the limitation of traditional toxicological evaluation on these newly detected environmental pollutants is because there are no extramural funds in NIH or EPA for this type of studies in the United States of America. That is why we ended up using studies from overseas to set up risk evaluations in the USA. This seems disturbing, specifically if we realize that the concentrations of these chemicals are estimated to be about 10-15 times higher in the biological fluids and tissues of American citizens as compared to European (specifically Swedish) citizens. I urge the responsible agents to encourage the classical toxicological evaluation of these compounds not in light of being similar in their structure to other compounds but in light of the fact that they are highly lipid soluble compounds that form depot in particular tissues of the ecological and mammalian biological systems. These depots create guaranteed life long exposure to these Xenobiotics, even after these chemicals are removed from the environment. The placental storage and transfer (if any) of these chemicals will turn them and their metabolites into trans-generational pollutants.

Richard Bull, Ph.D.

I do support the use of the neurodevelopmental studies for the purpose of deriving points of departure. As intimated above, however, considered alone, these endpoints have too little specificity to be of great concern. There are four fundamental issues: 1) The central importance of parallel neurochemical findings has not been used to advantage (or at least to the advantage it could be), 2) the interpretation of the neurobehavioral data as decreased habituation should be more critically evaluated, 3) the assessments of all the BPDEs depend upon results obtained from a single laboratory, and 4) the overwhelming application of uncertainty factors to such a subtle effect (i.e. relative to the usually accepted protocol) needs to be reconsidered. The first issue was addressed in question 1. The other three are discussed below:

It would have been better to present the actual behavioral data in the document rather than the habituation ratio. This ratio clearly is affected by both the depressed activity seen in the first period and the higher activity seen in the third period. The use of the habituation ratio forces an interpretation that may not be appropriate (or at least the reasons for selecting this parameter was not justified sufficiently in the documents or in the original papers). From the qualitative description of these data that was provided in these documents, they could be interpreted, with equal, if not greater, validity, as a depressed reaction to a novel environment and/or sustained hyperactivity.

Scientific findings need independent confirmation. Thus, EPA should be concerned about placing so much emphasis on set of studies that are generated completely within one laboratory, especially when the methodology and design are peculiar to that laboratory. Although it is not identified in the document, there is corroboration of the findings of Viberg and Eriksson with one compound (PBDE-99) in the study of Kuriyama et al. (2005). The experimental design was somewhat different. Nevertheless, the authors observed an increase in activity at PND 36 with a single dose of 300 µg/kg to the dam on GD 6. The measurement of activity after the animals had habituated to the test system, so the data are comparable to the activity observed in the 40-60 minute interval in the Eriksson et al. (2002) paper. Moreover, the lowest effective dose was somewhat lower than that reported by Eriksson and there is a clear NOAEL at 60 µg/kg.

It must be noted, however, that the implied relationship of the effects of PBDE-99 to altered thyroid function is not substantiated in Kuriyama et al. (2005). The doses producing the neurobehavioral changes occur at too low of a dose to be attributed to changes in thyroid hormone. In general, all the documents need to be more rigorous in their treatment of so-called "mode of action" data.

The application of group of uncertainty factors to a NOAEL despite the fact that the basis of this effect is not established and the apparent subtlety of the response relative to conventional developmental studies is not appropriate. This is discussed in some detail in the answer to question 1.5.

Lucio Costa, Ph.D.

Given the limited body of toxicological information available, use of the Eriksson/Viberg neurobehavioral studies as a basis for the health assessment is the proper approach.

Ralph Kodell, Ph.D.

The study of Eriksson et al. (2001) is the only available toxicity study with dose-response data on adverse (neurobehavioral) effects from exposure to BDE-47. The study of Viberg et al. (2004) has dose-response data on BDE-99. However, the studies of Branchi et al. (2002) and Kuriyama et al. (2005) also provide dose-response data. The data from Kuriyama were modeled and compared to the results from modeling the Viberg data, but the results from the Viberg study were selected for deriving the RfD. The reason for not using Branchi et al. (2002) for modeling is that there is an inversion at the highest dose. This does not seem to be a compelling reason to avoid modeling the data at the other doses. The study of Viberg et al. (2003a) is the only study with dose-response data on adverse effects for BDE-153. For BDE-209, the NTP rat and mouse bioassays (NTP, 1986) provide suitable data on noncancer endpoints as does the neurobehavioral study of Viberg et al. (2003b). Data from these studies have been evaluated and compared. There seems to be no alternative to basing the health assessment of the four PBDEs to a large extent on the Eriksson/Viberg studies, but the additional modeling for BDE-99 should be done and compared to Viberg (2004).

1.3 Are the Eriksson et al., 2001 (BDE-47), Viberg et al., 2004 (BDE-99), Viberg et al.,2003a (BDE-153) and the Viberg et al., 2003b (BDE-209) studies appropriate for determining the point of departure? Have the strengths and weaknesses of the Viberg and Eriksson studies been appropriately characterized and considered?

Deborah Rice, Ph.D., Chair

The characterization of the strengths and weaknesses of the Swedish studies is adequate for the most part. The exception, as stated above, is a major dependence upon an abstract with no supporting information, as well as accepting the authors' hypothesis concerning habituation. For 99, Kuriyama *et al.* and Talsness *et al.* are the appropriate studies upon which to base the RfD.

Ahmed Ahmed, Ph.D.

Following my review of the original reports, I found that Eriksson et al, 2001 (BDE 47), Virberg et al, 2004 (BDE-99), Virberg et al., 2003 (BDE-153) and Virberg et al, 2003b, 2003 (BDE-209) represent the most relatively complete studies on dose/response (neurobehavioral effects) relationships in animals. Most other available studies, discussed in these documents, could not directly correlate or tie the dose response and time course relationships. My main concern is that all these studies are coming from one group of scientists who pioneered the neurobehavioral / ADME (distribution in rodents) evaluation of these chemicals. With this information, come the ~~problems of lack of validation of data coming from one laboratory with other data coming form~~ other laboratories on the same scientific issues. Nevertheless, the authors of these reviews have clearly and transparently judged these studies without biased. They expressed the weakness of each study as well as its strengths in their utilization for driving the RFDs. The authors should be commended on their unbiased evaluation.

Richard Bull, Ph.D.

It is my opinion that these data are appropriate as long as it is emphasized that the neurochemical data that have been collected using parallel protocols add significant support to the conclusion that a modification(s) of the normal developmental pattern occurs as a result of these treatments. Please note that other neurobehavioral data were identified in the PBDE-99 document that should have been more formally considered as indicated in the response to question 1.2. Moreover, the data sets on activity per se are much more appropriate for dose-response assessment than the habituation ratio, for reasons provided above. The habituation ratio is derived data, but the data provide very little support for the idea that loss of habituation is the basis of these results.

Lucio Costa, Ph.D.

The studies by Eriksson and Viberg are unusual, as indicated in the reports, but are the only available for most BDEs. At this stage, they are the only ones available for determination of point of departure. However, the study of Kuriyama et al. (2005) should be considered for determination of point of departure for BDE-99. Strengths and weakness of these studies have been described appropriately (but see comments below). A sentence may be added to indicate that further developmental neurotoxicity studies are needed for BDEs.

Ralph Kodell, Ph.D.

The Eriksson et al. (2001) study appears to be the only study available with data that might be used to determine the point of departure for BDE-47. For BDE-99, data from several candidate studies are modeled for determining a point of departure. The Viberg et al. (2004) study appears to have the best dose-response data and to provide the best model fits. However, the data from Kuriyama et al. (2005) also fits acceptably and gives lower BMDLs for some endpoints. Reasons were given for choosing the Viberg-derived BMD over the Kuriyama-derived BMD, but I think the Kuriyama-derived value is equally justifiable. The only well-designed dose-response study with dosing both pre-natally and post-natally (Branchi et al., 2002) was not modeled because of an inversion at the highest dose. Conceivably, these data could be modeled for BMD estimation, perhaps by omitting the highest dose, as is sometimes done with cancer incidence data. The Viberg et al. (2003a) study is the only study with dose-response data for determining a point of departure for BDE-153. Both the NTP bioassay in rats and mice (NTP, 1986) and the study of Viberg et al. (2003b) in mice provide data appropriate for determining a point of departure for BDE-209. Of these, the Viberg et al. (2003b) study gives the lowest point of departure, and is thus selected.

A clear weakness of the Eriksson/Viberg studies is that they did not conform to health effects test guidelines for a neurotoxicity screening battery or developmental toxicity studies. The dosing regimen did not include gestation and lactation exposure, and only single doses were administered. More than one pup per litter was used for behavioral testing, thus confounding dose effects with litter effects. (Although the authors reported doing a split-plot analysis of variance in all four primary papers, which would correctly recognize and use the litter as the experimental unit for testing treatment effects, their pair-wise testing for such effects appears to ~~have treated each pup as an independent experimental unit.) In the cases of BDE-153 and BDE-~~209, the dose-response data were not considered suitable for statistical modeling because only graphical information was available. These weaknesses have been characterized and considered, and offsetting strengths have been discussed. However, it is surprising that the data on BDE-153 and BDE-209 cannot be recovered from the authors to allow dose-response modeling and BMD estimation. One important weakness that was not emphasized for BDE-47, BDE-153 and BDE-209 is that the Eriksson/Viberg mouse studies were done in males only.

1.4 Have the most appropriate critical effect and point of departure been selected? And has the rationale for the point of departure been transparently and objectively described?

Deborah Rice, Ph.D., Chair

For 47, 153, and 209, the appropriate critical effect was selected, although NOAELs and LOAELs are incorrectly identified (see below). For the BMD analysis for 99, EPA assumed that the number of pups was 8, which is completely inappropriate, and calls into question the results of these analyses. It is really surprising that the Agency would do this. It seems that the Agency wanted to do BMD analysis regardless of whether it made sense. Studies and endpoints were chosen according to whether they were amenable to BMD analysis rather that whether the decision made sense scientifically. This was the justification for using the habituation ratio, and was factor in use of the Swedish study for 99. This is letting methodology drive the science, and is inappropriate.

For 209 and 153, it is not stated whether the Agency requested the data required to perform BMD analysis. If not, this should be requested. If the investigators were unwilling to provide the information, this should be stated.

For congener 99, the studies of Kuriyama *et al.* and Talsness *et al.* should be used. A LOAEL of 0.06 mg/kg/day was identified for multiple endpoints, with no NOAEL. The Kuriyama *et al.* study reported effects on motor activity following a single exposure on GD6. Litters were treated appropriately, with one male and female per litter tested. Therefore this study does not have the problems of the Swedish studies, and is a much more appropriate choice than the Swedish study. The Agency dismisses the effects on spermatogenesis, even though the document states that sperm count needs to be reduced to a much greater extent in the rat than in humans to adversely affect reproductive success. This is inappropriate. Further, the LOAEL of 0.06 mg/kg/day should be used as the point of departure. Given that this is a LOAEL for several endpoints, the results of the BMD analyses should not be used since they are considerably higher.

Ahmed Ahmed, Ph.D.

With all the above consideration the authors have critically and objectively selected the most critical effect (neurobehavioral) and established the most appropriate point of departure (dose response) for all chemicals under review. The authors have very clearly rationalized, in great detail, in each individual review, their selection of each particular point of departures.

Richard Bull, Ph.D.

Among the data that are available, the neurobehavioral data provide the best data for identifying a point of departure. There are some lingering questions that relate to effects of BDE-99 that are reflected in histologic changes that occurred in the ovaries and vaginal epithelium at very small doses (i.e. 0.06 mg/kg day). However, these data were not described with sufficient clarity in the document to determine if they should not be used (i.e. neither incidence or severity are described in the context of dose-response).

My review of the Talness et al. (2005) study does raise some issues both about design and interpretation that may have been the basis of the Agency's apparent reluctance to use the Kuriyama et al. (2005) data on PBDE-99 (although it was not stated, if that were the case). For example, it is difficult to understand the conclusion that necrosis was observed by electron microscopy (Fig 1 & 4), but were not observable by light microscopy (see p. 194, section 3.1.2). Second, the number of animals examined for changes in the vagina was very small. Further, the authors do not make clear the basis for their repeated assertion that the doses tested resulted in levels of 6-29 times greater than reported in human breast adipose tissue. Was a human study conducted that looked at single doses that gave rise to such levels? I could find no reference to such a study.

Lucio Costa, Ph.D.

The most appropriate critical effect and point of departure have been selected and the rationale has been adequately described.

Ralph Kodell, Ph.D.

Although the seriousness of decreased habituation capability as a manifestation of an adverse effect on spontaneous motor behavior is not discussed, it is a common measure of developmental toxicity across studies. Thus, it appears to be an appropriate critical effect for deriving a point of departure. However, the individual measures of decreased habituation might be as appropriate as or more appropriate than the habituation-ratio as indicators of toxicity. For BDE-153 it is unfortunate that data on neither the habituation-ratio nor the swim-maze learning/memory test could be recovered for modeling. The dose-response for the swim-maze effect might be different from the habituation-ratio dose-response. (Unfortunately, swim maze data on BDE-99 (Eriksson et al., 2001) involved only a single high dose.) For BDE-209, too, it is unfortunate that dose-response data on the habituation ratio cannot be recovered for modeling and BMDL calculation. It's not clear why the actual data on BDE-153 and BDE-209 cannot be recovered from the studies' authors, given that the studies were published fairly recently (2003). In fact, it would be good if the dose-response data for all four PBDEs could be obtained so that litter effects could be handled properly in the BMD modeling. It would be far better if a BMDL rather than a NOAEL for habituation-ratio could be used for setting an RfD for neurobehavioral effects of BDE-153 and BDE-209.

For BDE-47 and BDE-99 and BDE-209, the rationale for selecting the point of departure in terms of the BMD and associated BMR are clearly spelled out. Selecting the BMD as the dose that corresponds to a shift of 1 standard deviation in the mean (BDE-47 and BDE-99) corresponds approximately to a 10% BMD with a critical cut-off defined by assuming 1% background risk for a normal distribution with constant variance. The use of a BMR of 10% for the BDE-209 quantal noncancer endpoints is explained. I think it ought to be stated explicitly that the BMDL rather than the BMD is used for these endpoints in order to account for experimental uncertainty (variation), which is a good practice and is related to the use of uncertainty factors. (However, the uncertainty may be understated because of treating littermates as independent experimental units.) Generally, for each endpoint, the BMD and BMDL resulting from the best-fitting model (or an average of the best-fitting models: BDE-209) and/or the model fitted to the most dose groups are selected. Then, the lowest BMDL among those is selected as the point of departure. The sequential likelihood-ratio testing approach for selecting the fitted model for neurobehavioral effects of BDE-47 and BDE-99 is very sound and is explained very clearly. However, I do not understand why, in the case of BDE-99, it must be assumed that 8 animals of each sex were tested behaviorally. Can't this be clarified by contacting the study's authors?

To the extent that data are available for dose-response modeling, I believe that the selection of critical effects and points of departure are appropriate, and that the rationale for the points of departure has been transparently and objectively described. However, I think a strong effort should be made to recover neurobehavioral toxicity data from the authors (Viberg et al., 2003a, 2003b) to allow dose-response modeling and BMD/BMDL calculations for neurobehavioral effects of BDE-153 and BDE-209, and to refine the modeling for BMD-47 and BMD-99.

1.5 Have the rationale and justification for each uncertainty factor (UF) selected in the draft 2 Toxicological Reviews of BDE-47, BDE-99, BDE-153 and BDE-209 been transparently described? If the selected UFs are not appropriate, what alternative UFs would you suggest and what are the scientific rationales for those suggested? Does the database support the determinations of the RfDs for BDE-47, BDE-99, BDE-153, and BDE-209?

Deborah Rice, Ph.D., Chair

The choice of UFs are not adequately justified, and are not appropriate in some cases. For all these RfDs, it must be remembered that motor activity is a screening procedure, not meant to be sensitive (or specific), and is a very crude measure of nervous system function. This is apparently not recognized by the Agency in the choice of less-than-default UFs.

BDE-47

UF_A and UF_H are appropriate.

The factor of 3 for "subchronic" to chronic is inappropriate. First, the exposure was actually an acute exposure. More importantly, the Agency repeatedly asserts that postnatal day 10 represents a unique critical window of vulnerability, and uses this as justification for the less-than-default value. The Agency cites no primary references documenting this assertion. Neither the published experiments of the Swedish group nor those cited as documentation include experiments addressing the issue. The literature review in the Ankarberg thesis cites a 1968 paper. A perusal of the Rice and Barone review of critical windows, cited by the Agency, reveals that multiple developmental processes are ongoing throughout the fetal and postnatal periods. "Spurts" in these processes, including brain growth, occur at different times for different endpoints in different areas of the brain. The fact that a particular day postnatally appeared more sensitive than two other postnatal days on one apical test (locomotor activity) in no way indicates that this represents a universally-sensitive period of development.

Another issue with respect to the choice of the subchronic-to-chronic UF is the tissue levels achieved following a single dose versus daily intake of that same dose. Even if PND10 did in fact represent a super-critical period in mouse development, exposure to the dam throughout gestation and to the pups beginning at birth would result in a higher body burden (including the brain) on PND 10 than a single exposure on PND10. It is possible, and maybe even probable, that levels of parent compound and metabolites would be more than a factor of 3 greater following repeated exposure than following a single exposure. Therefore a factor of 3 cannot be justified. It is also important to realize that PND10 in a mouse represents prenatal exposure in a human, which should be discussed in these documents in relation to choice of UF_S. The criticism of the literature ~~review with respect to potential~~ accumulation of ~~toxic metabolites following long-term exposure~~ under General Question is also relevant to the inadequacy of 3 as an UF from a single-dose study to lifetime daily exposure.

The UF_D is overly conservative, and should be decreased to 3. Although a prenatal developmental study was not performed, the postnatal behavioral study (representing prenatal human exposure) should be a sensitive measure of toxicity. It is unlikely that reproductive studies would identify effects at lower doses.

$$0.35 \times 10^{-3} \div 3 = .00011 \text{ mg/kg/day} = 0.1 \text{ ug/kg/day}$$

So far, the RfD is not different from the EPA calculation. However, it must be noted that the BMDL is being treated as a NOAEL, which it is not. It is the lower limit on a defined effect level, and so is comparable to a LOAEL. An additional factor of 3 should be included to go from a LOAEL to a NOAEL, which is considered adequate given that the starting point is the BMDL rather than the BMD.

BDE-99

The Kuriyama *et al.* and Talsness *et al.* studies should be the basis of the RfD. The results of the BMD analysis should not be used, since a LOAEL considerably lower than this was identified on multiple endpoints.

UF_A and UF_H of 10 are appropriate.

UF subchronic to chronic should be 10 (see above).

An UF of 10 should be applied to go from a LOAEL to a NOAEL.

An UF_D of 10 is not necessary. The effects of both prenatal and postnatal exposure on behavior and reproductive function are available from several studies, including aspects of the FOB in the German study.

$$0.06 \text{ mg/kg/day} \times 10^{-4} = 6\times10^{-6} \text{ mg/kg/day} = 6\times10^{-3} \text{ ug/kg/day or } .006 \text{ ug/kg/day}$$

BDE-153

There was a statistically-significant effect at the low dose of 0.45 mg/kg at six months of age; therefore this dose is not a NOAEL but a LOAEL. In addition, examination of the figures revealed a monotonic dose-response relationship for a number of measures, that was not statistically-significant at the low dose. This suggests that effects were produced at this dose. The Agency offers no rationale for ignoring these results. It must be recognized that animal studies usually have very low power to detect an effect; therefore Type 2 errors are often of more concern than Type 1 errors. That is particularly relevant in situations like this where there is a clear dose-response relationship, including at non-significant lower doses.

The UF_A and UF_H of 10 are appropriate. The UF for subchronic to chronic should be 10 (see above). A UF for extrapolation from a LOAEL to a NOAEL should be applied. Given the minimal statistical significance at the lowest dose, 3 is appropriate. The UF_D should be 3

$$0.45 \text{ mg/kg/day} \times 10^{-4} = 4.5\times10^{-5} \text{ mg/kg/day} = 4.5\times10^{-2} \text{ mg/kg/day or } 0.05 \text{ ug/kg/day}$$

BDE-209

For 209, 2.22 is not a NOAEL, but a LOAEL. There were effects at this dose that were statistically-significantly different from control, and examination of the figures revealed a dose-dependent trend even for measures that were not significant at the low dose. There is no rationale provided in the document for ignoring these significant findings. Moreover, the LOAEL in the rat study was 6.7 mg/kg, very close to the 2.22 mg/kg in the mouse study, with no NOAEL identified.

The UF_A and UF_H of 10 are appropriate. The UF for subchronic to chronic should be 10. An UF for extrapolating from a LOAEL to a NOAEL should be 3. The UF_D should be 3.

$$2.22 \text{ mg/kg /day} \times 10^{-4} = 0.2 \text{ ug/kg/day}$$

Additional comment

Presenting data for each congener in isolation fails to provide a comprehensive synthesis of the literature. In particular, the effects on motor activity have been described in 7 congeners in mice, as well as in the rat for 209. Some of these studies were performed in laboratories other than the Swedish lab. Reference in the documents to "one study" is therefore somewhat misleading. Although the Agency may still rate confidence in these RfDs as "low", it should not imply that the motor activity results are somehow isolated findings. The same argument may be made for other endpoints.

Ahmed Ahmed, Ph.D.

In their calculation of each individual RFD for each PBDPE, the authors have clearly classified several uncertainty factors for each compound based on the available information in the studies utilized. I found that their selection of these uncertainty factors to be well rationalized and the objectivity of each uncertainty factor to be very clear. It was apparent that the number assignment was very uncertain during the panel meeting on Feb 22,2007. It seemed very uncertain whether several UFs should be assigned a10 or 3.

In considering acute versus chronic uncertainty factor, I feel that the accumulation of BDEs, specifically the lower brominated compounds, tetra (BDE-47 and penta (BDE-99) should be considered in the calculation of their RFDs. These compounds detected in various human tissues and biological fluids and have very long half lives in human tissues; the adipose tissues in vital organs and biological fluids; breast milk. Thus, for the highly susceptible human groups such as fetuses and infants there will be continuous internal dosing that is coming from storage depots. Accordingly, the body burden for infants will not be only dependant on exposure to external dosing from the environment. It will be dependant on a combination of external (environmental) and internal factors (the depot of biological tissues and fluids). This complexity should be considered in the estimation of RFDs. Specifically for the U.S. population. In the American population, the levels of most of these chemicals in blood, tissues and biological fluids are about 10 or more times higher than that detected in biological fluids from other (European) countries. Such facts should be considered in the calculation of RFDs here in U.S.A. Finally I believe that available limited data base should support the determination of the RFDs for BDE 47, BDE 99, BDE 153, and BDE 209.

Richard Bull, Ph.D.

The rational and justification of each UF has been transparently described. However, I believe that they have been inappropriately applied to these chemicals.

There was no consideration in the document related to the specificity and sensitivity of the neurobehavioral and neurochemical measures that have been applied vs. more standard endpoints. In particular, it is inappropriate to apply the UF relative to data base inadequacies. One might consider modifying UFA and UFH as well.

Given the nature of the available data, the rationale for using an adjustment from subchronic to chronic exposures (UFS) for these data is also not sustainable scientifically. In this case, the critical issue is whether the body burden of parent compound is important. Thus, the adjustment of 3 that is made on the UFS is not appropriate. Rather one needs to consider the extent to which the mother's pre-pregnancy accumulated body burden would influence the developmental outcome. As I see no way of even making a judgment on this issue based on the available data, I suggest that UFS be raised to 10.

There is a more general problem with the database uncertainty factor when it is applied to the development of RfDs. The traditional across species and within species uncertainty factors relate to the critical endpoint being addressed in the risk assessment. The database uncertainty factor addresses questions that go beyond this endpoint and focus on risks that might occur, but there are no relevant data. Thus, it does not reflect on the accuracy of the assessment of the endpoint being evaluated. This uncertainty factor is more appropriately applied at the point that risk management decisions are being made (e.g. at the point that MCLs are being developed). This concern should be introduced at the point where other parallel uncertainties are entertained (e.g. can remediation efforts reduce the risk or whether the MCL is within a range that can be measured).

Lucio Costa, Ph.D.

The selection of UFs has been described in detail, though I do not fully agree with some choices (see comments below for individual BDEs). The database on which RfDs are determined is in most cases very poor, particularly in case of BDE-47 and BDE-209. Perhaps RfDs should be acknowledged as "temporary", while waiting for additional studies that may increase confidence.

Ralph Kodell, Ph.D.

Default uncertainty factors of 10 for UFA and UFH are used for BDE-47, BDE-99 and BDE-153 without much explanation or justification. For BDE-209, the UFA default (but not the UFH default) has been explained satisfactorily. Taken together as a product, values of 10 each for UFA and UFH may be overprotective, but there is no alternative methodology that is currently accepted for expressing these factors as a smaller unitary factor, as might eventually be done via hierarchical modeling.

Looking at these factors separately, a UFA of 10 might at first seem conservatively large given that no evidence of an association between neonatal exposure to PBDEs and neurobehavioral effects in humans exists. On the other hand, there is no evidence to the contrary, and the mode of action is not yet understood. Because the potential adversity to humans is present, a value of 10 seems justifiable in all four cases. For UFH, I believe there is justification for deviating from the default value for all four congeners. Because the neurobehavioral effects seen in rodent studies result from exposures at critical points in early development, I believe it can be argued that the most sensitive members of the population for these effects (neonates) are already accounted for. Because the default value of 10 is used to account for differences in sensitivity among all members of a population, and because it seems hard to justify a factor that large for variation just among neonates, a smaller value of UFH appears justified. I recommend a value of 3 for UFH for all four PBDEs.

The choice of 3 for UFS for all four congeners appears justifiable to me, recognizing that timing of exposure is more critical than duration of exposure for the neurobehavioral effects observed. However, I regard this factor as accounting more for uncertainty arising from a lack of pre-natal exposure in the studies used to derive the RfDs than for uncertainty regarding potential effects of chronic exposure.

Using a value of 10 for UFD for BDE-47, BDE-99 and BDE-153 does not seem justifiable. In my opinion, if the database is so uncertain as to require a UFD value of 10, then the database is too limited to allow the derivation of meaningful RfDs. The primary neurobehavioral endpoint appears to be quite sensitive, and it is consistent across congeners. For BDE-47, I recommend a UFD value of 1. Although there is only a single study, the neurobehavioral endpoint is the same as for the other congeners, and dose-response data are available for basing the point of departure on a BMDL. For BDE-99, I also recommend a UFD value of 1. There are several studies and dose-response data are available for basing the point of departure on a BMDL. For BDE-153, I recommend a UFD value of 3. There is only a single study, and dose-response data could not be recovered for BMDL calculation. If those data can be obtained from the study's authors and used for BMDL calculation, then this factor could be reduced to 1. For BDE-209, I recommend raising the factor from 1 to 3. Granted, there are data from more than one study, and BMD modeling was done along with model averaging for non-neurobehavioral effects. However, a NOAEL for neurobehavioral effects rather than a BMDL was selected for the point of departure, because of the inability to recover the neurobehavioral dose-response data. To me, the absence of definitive data for dose-response modeling for neurobehavioral effects reflects an inadequacy in the database, and in fact, inadequacy in the very data ultimately used for deriving the RfD. If data can be obtained from the study's authors and used for BMDL calculation, then this factor could be reduced to 1.

One factor that is not mentioned is UFL for going from a LOAEL to a NOAEL, because LOAEL-to-NOAEL extrapolation is not done here. However, I think this factor should also apply when using a BMDL10 as a point of departure. A 10 % benchmark response is not negligible. A BMD10 (BMDL10) is more in line with a LOAEL than with a NOAEL. I recommend applying a UFL factor of 3 to each of the BMDL10 values to account for uncertainty in extrapolating from a dose of non-negligible toxicity to a dose of negligible toxicity.

I believe the database supports the determinations of RfDs, but I agree with the statements in the documents that the overall confidence in the RfD assessment of BDE-47, BDE-99 and BDE-153 are low. I feel the same way about BDE-209.

2. BODY BURDEN APPROACH

2.1 Are there adequate data for considering body burden as an alternative dose metric to administered doses in any of the RfD derivations?

Deborah Rice, Ph.D., Chair

There are high-quality studies on the body burden of these congeners in humans, as well as in food and the indoor environment. (Exposure is not addressed in these draft documents.) These data are sufficient to estimate the relationship between exposure and body burden in humans. However, toxicity data in humans is lacking. The converse is true for experimental studies: toxicity data are available, but not in relation to body burden. Therefore a body-burden approach cannot be used at this time.

Ahmed Ahmed, Ph.D.

The current available animal and human data regarding the body burden of BDE's are sporadically designed and extremely limited. Although there are several studies under each compound that describe the ADME or body burden concept (absorption, distribution and tissue accumulation and excretion), the kinetics (t1/2, volume of distribution, rates of absorption, metabolism and excretion) of the absorption, accumulation and removal processes of each individual compound have not been established. Similarly the identity, type and structure of the accumulated chemical species have not been recognized. In natural environmental exposure setups, there is no single (exposure) dose. Humans are continuously exposed, continuously storing, distributing, metabolizing and excreting the compounds or their metabolites. In this regard even the year or more long half life, described for some congeners, is in reality not a true kinetic factor, because the parent molecules or its metabolites are primarily stored in certain target tissues and continuously released into the blood for circulation, metabolism and excretion. These tissue stores are continuously replenished by absorbing more from the external surrounding environment. All these events should be taken when considering body burden as an alternative dose metric in the derivation of any of the RFDs. Such information is currently scarce (McDonald, 2005).

Richard Bull, Ph.D.

There may be a reason for considering body burden. As indicated in the response to questions 1.1 and 1.5, the question of whether increased body burden would contribute to the critical neurobehavioral endpoints evaluated has simply not been tested. It is for this reason that treating a single dose experiment as if it were a subchronic exposure is inappropriate. In addition, it is not clear whether the body burden or daily dose is the best dose metric for the chronic effects of those members of the PBDE class that have been evaluated in chronic studies. Therefore, this question also depends upon the endpoint that is being evaluated and the documents have not provided a basis for either approach. There are huge inconsistencies in the ADME among the PBDEs. Chronic exposure would appear to lead to large body burdens with some of the PBDEs, but not others. Furthermore, simply showing that the compound, a metabolite, or a radiolabel derived from that compound reaches its target site does not establish a causal link. For the developmental effects, in particular, the question of whether levels of the parent compound or a metabolite is the most appropriate dosimeter has to be resolved experimentally, not guessed at. As a start, the variability in the extent of metabolism across these four PBDEs needs to be evaluated to see whether the neurodevelopmental effects appear to occur at similar body burdens of the parent compounds. That is about as far as an analysis could be taken given the data that are available.

The above points are critical as the only compound for which there are cancer data is BDE-209, which appears to be metabolized and excreted much more rapidly than the PBDE's with lower bromine substitution. It does not bioaccumulate to the extent of the other compounds. Therefore, even this chronic effect may not be a function of the body burden. Part of this may have resulted from the lack of context provided for the metabolism & kinetic data that were provided. There are several aspects of the write-ups that suggest that data to this effect may exist, but were simply not critically and/or creatively interpreted or used by the authors of the document. Some of these issues are discussed in greater detail in the editorial comments provided below. To make proper use of the available metabolism and kinetic data that are available requires an integrated assessment of all four compounds. Therefore, one questions why these chemicals are addressed in four separate documents.

Lucio Costa, Ph.D.

Body burden would be an alternative dose metric to derive RfDs, however, current available data are still too limited, in my opinion.

Ralph Kodell, Ph.D.

There are not adequate data for considering body burden as an alternative dose metric to administered dose.

2.2 Do you agree with the rationale described in the Toxicological Review of BDE-99 that the data on the window of susceptibility of the cholinergic receptors to BDE-99 tend to minimize body burden concerns?

Deborah Rice, Ph.D., Chair

Absolutely not. The MOA of changes in motor activity may or may not be related to cholinergic activity. Perturbation of multiple neurotransmitter systems affects motor activity, and other systems have not been looked at with respect to PBDEs. In addition, no primary studies are cited documenting a "super-critical" window of susceptibility for effects on brain development, including development of the cholinergic system.

Ahmed Ahmed, Ph.D.

Even though I don't completely agree and don't understand clearly the question, I have to accept the concept. That is because any experimental design has to have an assumption that is based on the available information. We know from the literature that the fetal and neonatal brain developments are different in rodents and humans. Therefore, fetal and neonatal cholinergic receptors regulation (up or down) could also be different. While brain development in rodents occurs during postnatal periods, it occurs in utero in humans. Both conditions have extremely different manifestations regarding nutritional, environmental exposure and other toxicokinetic parameters. Therefore, to focus on a specific and certain particular time for susceptibly (PND 3, 7 or 10) for cholinergic receptors in neonates may increase the uncertainty factor in the RFDs' calculation.

Richard Bull, Ph.D.

I am not sure that I understand this question. There is no direct evidence provided that BDE-99 treatment directly affected cholinergic receptors that I could identify in the document. What was presented was an indication that animals treated neonatally with nicotine were responsive to the "loss of habituation" following dosing with BDE-99 at 8 mg/kg at 5 months of age. The effect was not produced by nicotine pretreatment alone, or by only administering BDE-99 at 5 months of age. This is not evidence of an interaction at cholinergic receptors! On the surface, the data ~~obtained with preadministration of nicotine appears to actually separate the mechanism of~~ nicotine from that of BDE-99. The nicotine effects are actually inverted (i.e. suppressed activity) with nicotine at higher doses. Why do neither BDE-99 or nicotine, administered alone, produce the effect when administered at 5 months? The mechanism of the interaction must be complex and indirect.

The second part of the story is that nicotine treatment at PND 10 caused decreases in binding sites for bungarotoxin and QNB, that specifically bind to nicotinic and muscarinic subtypes. A similar effect was observed with BDE-99 administered at PND 10. It is unlikely that the effects of BDE-99 are an expression of an interaction at nicotinic receptors, per se. Binding to such receptors has structural requirements not remotely met by BDE-99 or any of its likely metabolites. Whatever BDE-99 does must involve a less direct mechanism. That could be an inhibition of the expression of these receptors, but just as likely, it could mean that there is a deficit of neurons that express these receptors. If the document goes into mode of action questions, it is imperative that it clearly distinguishes among alternative mechanisms that are possible. One of those criteria clearly has to be a consistency in the doses required to produce the effect and that needed to activate a particular mechanism thought to be a key event in the mode of action. If one mechanism is considered to be more probable, the reasons for this conclusion need to be explicitly stated. Otherwise the document has to conclude that the mechanism of these effects have not been established.

Lucio Costa, Ph.D.

Question is unclear.

Ralph Kodell, Ph.D.

The hypothesis of impaired development of the cholinergic system during the postnatal "brain growth spurt" period as an explanation of the neurobehavioral effects seen in the Eriksson/Viberg studies is plausible. Staskal et al. (2006b) showed that brain levels of BDE-47 administered to neonatal mice on PND 10 were higher than levels in adult animals. Branchi et al. (2002) showed significantly elevated brain levels of BDE-99 in mice administered a high dose from GD 6 to PND 21. Eriksson et al. (2002) also showed that radiolabeled BDE-99 can be taken up and retained in the neonatal mouse brain, although the amount of radioactivity in the brain was only between 0.4% and 0.5% of the administered dose. Viberg et al. (2003b) reported a similar result for BDE-209. The limited data available on BDE-99 indicate that the effects on habituation were seen only at doses that also cause decreased binding of the cholinergic receptor antagonists. For BDE-153, Viberg et al. (2003a) showed that the density of nicotinic acetylcholine receptors in the hippocampus of 6-month old mice treated on PND 10 was significantly decreased at 9.0 mg/kg, a dose at which mice showed significant defects in learning and memory. However, there are no definitive data on mode-of-action. PBDEs have some structural similarity to the thyroid hormone T4. It has been suggested that they may interfere with thyroid hormone transport by competitively binding with one of the transport proteins in plasma. Although it is known that thyroid hormones are essential for normal brain development in humans and that decreases in thyroid hormone levels during fetal and early neonatal life may have profound adverse effects on the developing brain, thyroid hormone levels and behavioral activity were not co-measured in any of the developmental toxicity studies in mice or rats. Although the data on the window of susceptibility of the cholinergic receptors to the PBDEs (PND 3 – PND 10) are suggestive, I believe there are too many other possibilities for mode of action for this rationale to minimize body-burden concerns.

3. QUESTIONS RELATED TO THE CARCINOGENICITY ASSESSMENT OF BDE-209

3.1 Is the weight of evidence for the carcinogenicity of BDE-209 in the draft Toxicological Review appropriately described? Are there additional studies that should be included?

Deborah Rice, Ph.D., Chair

The Agency needs to address the issue raised in the public comments concerning the change in criteria for the identification of tumors since 1985. If regenerative nodules are being included in the count of lesions, and these would not progress to cancer, then the analysis may be flawed. The doses in these studies were very high, and undoubtedly resulted in liver toxicity, but that does not necessarily mean 209 produces hepatocarcinogenicity. The Agency presumably is aware of this change in criteria, and yet does not discuss it or justify why it is not relevant.

Ahmed Ahmed, Ph.D.

The weight of evidence on the carcinogenicity of BDE 209 in the draft toxicological review is based on a carcinogenicity studies that were conducted more that quarter of a century ago. Although the authors of the draft review document have provide a methodical and complete description of the studies, the study itself and its results leave a lot to be desired. Modern, molecular and more sensitive biomarkers of cancer should be implemented in future carcinogenesis studies for BDE-209 and other congeners. The current available studies had shed some doubts regarding the pre-carcinogenic effects of BDE 209. The studies utilized very high doses which lead to some toxic effects and increased animal deaths.

Currently I am not aware of any recent study that addressed the carcinogenicity of BDE-209.

Richard Bull, Ph.D.

Yes.

Lucio Costa, Ph.D.

The weight of evidence for carcinogenicity of BDE-209 is appropriately described. I am not aware of any additional studies.

Ralph Kodell, Ph.D.

The weight of evidence for the carcinogenicity of BDE-209 is appropriately described. I do not know of additional studies that should be included.

3.2 Do the data support estimation of a cancer slope factor for BDE-209? If yes, is the rationale for the quantitative analysis objectively and transparently described, considering the uncertainty in the data and the suggestive nature of the weight of evidence? Have the rationale and justification for the use of linear low-dose extrapolation been objectively and transparently presented?

Deborah Rice, Ph.D., Chair

See 3.1. This issue must be resolved. However, I am not so concerned about the thyroid effects. Congener 209 does in fact affect thyroid function, at least after developmental exposure (Rice et al, in press).

Ahmed Ahmed, Ph.D.

The available data supports the estimation of a cancer slope factor for BDE-209. The rationale for the qualitative analysis was objectively and transparently described. Similarly the justifications for the use of linear low dose extrapolation have been objectively presented.

Richard Bull, Ph.D.

After reading the public comments directed at treatment of the carcinogenesis data that is available on BDE-209, it is apparent that there are a variety of problems with the NTP data. Comments from industry focused on the fact that the responses were fairly modest and that the criteria have changed for classifying liver lesions in the rat since this study was completed. I am less concerned with the scoring nodules as tumors. Nodules generated in initiation promotion protocols are known to regress with suspension of treatment. This is much less likely to happen with chronic studies of a single compound.

However, I question the appropriateness of the original NTP study for developing risk estimates in general. The very high concentrations were provided to the animals in the diet make it almost certain that the external dose is not a reliable indication of the systemic dose. The extremely low solubility of BDE-209 in aqueous media (<0.1 ug/L) suggests that the transfer rate from food to aqueous phase would sharply limit to absorption proportional to external dose to much lower concentrations than the 25,000 and 25,000 ppm in the diets used in the NTP study. The document contains data indicating that absorption is sharply curtailed at much lower concentrations in the diet (see quotation of studies of El Dareer et al., 1987) and the fact that much higher percentages of absorption were derived from the gavage dosing of much smaller doses of PBDE-209 (see Sandholm et al. 2003; Morck et al. 2003). These observations are supported by the more uncertain studies of the absorption of the labeled compound. While there were some evidence of tumor induction in both mouse and rat studies, there was little indication of dose-response, suggesting that the response was limited by absorption. If this is the case, the true point of departure for estimating cancer risk could be order of magnitude lower than is suggested by the doses administered. For this reason, revisiting the results of the NTP studies will be a waste of time and money. I would strongly suggest that a new bioassay be conducted that can be more easily related to environmental exposures. The doses administered in such studies should be established based on better designed studies of absorption, distribution and metabolism than have been conducted to date and development of a first generation PBPK model.

Lucio Costa, Ph.D.

Data are indeed suggestive of a carcinogenic potential of BDE-209. BDE-209 does not appear to be genotoxic (though database is limited), but no clear indication of possible epigenetic mechanism is available. On the other hand, chronic toxicity studies suggest the induction of non neoplastic or pre-neoplastic lesions in target organs. The linear low dose extrapolation as a default, conservative approach appears justified in this case, as is the classification of BDE-209 as a possible human carcinogen.

Ralph Kodell, Ph.D.

The data appear to support estimation of a cancer slope factor for BDE-209 based on neoplastic nodules or carcinomas (combined) in the livers of male rats (NTP, 1986). This conclusion assumes that any change in the classification of neoplastic nodules that might have taken place subsequently would not change the dose-response appreciably. The rationale for the quantitative analysis is transparently described. The cancer data are characterized as providing "suggestive evidence of carcinogenic potential," in keeping with the EPA cancer guidelines (EPA, 2005a). The modeling of several tumorigenic endpoints leads to selection of the cancer slope factor corresponding to the most sensitive endpoint (liver nodules/carcinomas). I did not see a rationale or justification for the use of linear low-dose extrapolation, except for a reference (page 62) to two EPA guidelines documents for cancer assessment (EPA, 2005a, 2005b).

3.3 Are there alternative modeling approaches that should have been considered instead of or in addition to the linear low-dose extrapolation approach?

Deborah Rice, Ph.D., Chair

There are insufficient data to consider alternative approaches.

Ahmed Ahmed, Ph.D.

To my knowledge the authors have explained all possible modeling approaches. They selected the best fit model for their interpretation of the experimental data. I commend the authors' consciousness for siting the drawbacks of these studies and for the thorough analysis of the available data.

Richard Bull, Ph.D.

There are no data that would permit departure from linear low-dose extrapolation. As indicated above, I am concerned about the very high doses that were used in these studies. It is not clear that absorption would be linear with dose because of the solubility problems that are discussed in more detail in the editorial comments that have been appended to these responses to EPA's specific questions.

Lucio Costa, Ph.D.

Data are indeed suggestive of a carcinogenic potential of BDE-209. BDE-209 does not appear to be genotoxic (though database is limited), but no clear indication of possible epigenetic mechanism is available. On the other hand, chronic toxicity studies suggest the induction of non neoplastic or pre-neoplastic lesions in target organs. The linear low dose extrapolation as a default, conservative approach appears justified in this case, as is the classification of BDE-209 as a possible human carcinogen.

Ralph Kodell, Ph.D.

Other modeling approaches could have been considered, but I don't think that they necessarily should have been considered. The liver dose-response data are quite linear and there are only two nonzero doses plus a zero-dose control. The linear model fits quite well. It seems likely that other dose-response models would give similar fits. It's possible that such models would extrapolate differently from the linear model below the data, but it is my opinion that the data themselves are not informative enough to justify a different, say, sub-linear, extrapolation approach.

MISCELLANEOUS REVIEWER COMMENTS

Ahmed Ahmed, Ph.D.

Comments on Each Document:

BDE 47:

1. Page 7; 3.2.1: Current Human data regarding distribution and disposition of BDE 47 is spotty, sporadic with low number of samples and uncontrolled health and environmental conditions, with no regard to geographical or ecological circumstances.

2. Human data should be summarized and presented in a comprehensive table with references in this and in all other documents.

3. Page 13; 3.2.2: Animal data on the disposition of BDE-47 focused on several 14C labeled compounds. In most of these studies, the position of the label was not mentioned, the purity of the 14C-compound was not known, the specific activity of the compound was not given and the ADME studies were based on following the radioactivity in various tissues and biological media. No pharmacokinetic parameters were estimated from these studies.

4. The identity of the detected radio labeled species in tissues and biological fluids is very important to clarify whether this species is the parent molecule, a metabolite or even a carbon dioxide molecule.

5. The levels of radioactivity should be uniformly expressed throughout this document and other documents. That is essential to be able to do reasonable comparisons among various congeners. Concentrations as mg-equivalent / g tissue/g lipid weight should be used across the document.

6. I suggest that the authors to put some proposed metabolic pathways for this compound. It could be extracted from other brominated congeners such as BDE-99. The proposed metabolic pathway similar to that presented for BDE-99 could be used here too. This will strengthen the fact that this and other lower brominated congeners could be obtained from higher brominated ones.

Mice are known to have higher levels of various CYT P450 enzyme activities than rats. This should be reflected in the discussion of the differences in the disposition, metabolism and excretion of this compound and other congeners.

8. Extensive explanation of receptor site interaction is somewhat confusing due to the lackluster effects of these compounds on various receptors. It would be beneficial if a summary table is presented either in the beginning or at the end of this section. Relative potency of various congeners on specific receptors should be indicated.

9. A table, in page 39, that could summarize the neurobehavioral, developmental and reproductive effects of BDE-47 should be added. It will show how Eriksson et al represent as complete a study to be used in RFD determination. It will be helpful if in each document a similar table is inserted before the selection of the principal study as in case of the document of BDE-99.

10. The Uncertainty Factors for population at risk (fetuses and newborn) and for conversion from single dose to multiple and continuous routes of exposure should be adjusted for, as described before.

11. The neurobehavioral studies that are utilized in RFD evaluation have limited end points and were conducted in one Swedish research location. Due to the lack of complete dose response/ time course studies, I have to agree on using them in the determination of the corresponding RFD. My agreement is based on the fact that these studies have statistically significant end points for neurobehavioral adverse effects within the framework of the experimental design.

12. A major concern about the experimental design, described in these studies, is ignoring the "letter effect". The authors of the study should have used offspring from multiple letters rather than from one letter. Randomization was based on only two letter and randomization approach was not described.

13. Although radioactivity was detected in brain, in the studies, there was no explanation in which brain areas radio activity was detected. Anatomical or histological localization of the radioactivity would have added significant weight to the mechanisms of the observed neurobehavioral studies.

14. There seems to be no correlation between the postnatal day of exposure and the concentration in the brain. Exposure at PN Day 10 provided the brain with the highest concentration while had no increase in neurobehavioral adverse effect.

BDE-99

1. The table in page 58 is an excellent summary to the developmental and reproductive effects of several BDEs. It shows how Viberg et al (2004a) represent as complete a study to be used in RFD determination. It will be helpful if in each document a similar table is inserted before the selection of the principal study for RFD estimation.

2. Study of Kuriyama et al (2005) showed some good dose-response relationship for neurobehavioral as well as male reproductive effects. This study should be considered in the determination of RFD for BDE-99.

3. ADME evaluations in animals are un-objectively presented. They were presented as several summaries of several studies but with no connection and with limited interpretations of the data. The proposed metabolic pathway presented in page19 is very helpful. Similar pathway should be presented for other congeners.

4. Due to the metabolic relationship between higher and lower congeners of BDE, a comprehensive metabolic profile for all of these compounds should be presented in every toxicological review for each individual BDE.

5. Comments on the radioactive compound, its purity and specific activity that are described before, will also apply for this and every other congener.

6. There are large number of receptor studies that are presented in the document. A comparative summary with references will be helpful for the reader to easily conclude which is the most sensitive receptor for this and other congeners.

7. Concerns regarding Uncertainty Factors described before, apply here, too, for BDE-99.

BDE-153

1. Human distribution studies are somewhat sporadic and most of them were designed for the detection of other chemicals. The data in table 5 should be expanded to include BDE- 209. This table should be presented in the document of every congener.

2. I would suggest that the authors of the document should create a summary of values for the concentration of various PBDs in human tissues in various geographic locations. Schecter et

al (2003) showed that the mean median concentrations of BDE in Texas are much higher than any other places in USA or Europe.

3. A summary table for receptor studies is needed.

4. Comments about 14C ADME studies described before apply here too.

5. Need to insert comprehensive metabolic pathway similar to that in BDE-99 document.

6. In most of the in vitro and in vivo animal studies that are presented in these documents, oily vehicles were used (corn oil etc.). I found this problematic. That is because large number of bromine atoms on a phenyl ring imparts several electrophillic and lipophilic properties to the aromatic ring. The increased lipophilicity will significantly alters the distribution and tissue uptake of BDE between the oily vehicle and the biological system with its hydrophilic / lipophilic properties. These conditions lead to decreased absorption and distribution with subsequent alteration in metabolism and excretion with little correlation to real occupational and environmental conditions.

7. Rational for driving RDF and Conclusions are appropriate and transparently presented. A summary table for all available studies that could be used for the estimation of RFDs should be included. This table will clarify why a particular study was the most appropriate for the estimation of RFD.

BDE-209

1. The cancer risk derived for BDE-209 is based on very high doses utilized in a two and half decade old study. These doses could not be occupationally or environmentally possible except in accidental conditions.

2. Like other toxicological reviews of other BDEs, ADME evaluations in animals are un-objectively presented. There are several summaries of several studies but no connection and limited interpretations of the data. The proposed metabolic pathway presented in for BDE-99 is very helpful. Similar pathway should be presented for this and other congeners.

3. Due to the conversion of higher molecular weight BDEs (those with larger numbers of bromine atoms) metabolic relationship between higher and lower congeners of BDE exists. Therefore, a comprehensive metabolic profile of all these compound should be presented in every toxicological review for each individual BDE.

4. Comments on the radioactive compound, its purity and specific activity that are described before, apply for this and every other congener.

5. Extensive number of receptor studies is presented in the document. A comparative summary with references will be helpful for the reader to easily conclude which is the most sensitive receptor for this congener (and other ones).

6. Concerns regarding Uncertainty Factors described before, apply here for BDE-209, too.

Richard Bull, Ph.D.

Editorial comments:

1. The Agency should reconsider the traditional organization of these review documents. The old organization is becoming very cumbersome as more and more data become available that bear on the issue of mode of action or corroborating data that support the documents overall conclusions. In this particular set of documents, the artificial separation of the neurobehavioral studies and neurochemical data over three categories (reproductive/developmental studies, neurotoxicity and Other studies) really made these difficult documents to review. I suggest that all of the data that contribute to a cohesive understanding of a particular toxicological effect need to be included in the same section. To pick a specific case, all data relevant to the neurodevelopmental effects of BDE-99 should be presented together, whether the data relate to neurobehavioral, neurochemical, or gene expression data in the CNS.

Related to this point, it is also suggested that conclusions that are derived from explorations of alternative modes of action for a particular effect be expressed more categorically. For example, there have been some investigation of contribution of thyroid hormones changes to the neurodevelopmental effects of the BPDEs. The only clear results with respect to the thyroid hormones is that of Zhou et al (2002), where effects of a different mixture (DE-71, a mixture of tetra and penta PBDEs) on thyroid hormone levels were described. The doses required to produce such effects were not far off those that produced neurodevelopmental effects with BDE-47, but were much higher that the doses of PDE-99 that produced neurodevelopmental effects. Thyroid hormone levels were examined in a study of adults treated with BDE-47 by Hallgren and Darnerud (2002), but only FT4 was reduced, not thyroxine, and the dose required to produce this effect was much too high. Other studies with the PBDEs appear to be negative, but in some cases the actual doses utilized were not provided in the document (e.g. the Hakk et al. 2002 study cited in the BDE-99 document). To this reviewer there is no basis for suggesting that the neurodevelopmental effects observed with the PBDEs are related to thyroid hormone-related effects. This actually raises concerns, rather than lowering them. If a thyroid hormone-based mode of action were identified, there would be less of concern because the risks associated with this mode of action are reasonably well understood. Therefore, a clear conclusion should be drawn that says it appears unlikely that modified thyroid function plays a role in the neurodevelopmental effects observed with this class of compounds. Similar statements should address other modes of action that have been found to be consistent with or inconsistent with respect to particular toxicological effects. In the absence of a particular toxicological effect, these data are of little use. It is really important to begin to make these distinctions as the "presumed mode of action data" may frequently form the bulk of the available data on a compound and this information needs to be placed into better context.

2. The data on PBDE occurrence in biological samples involve relatively small populations and may not be representative of either the U.S. or the World populations. Nevertheless, there are observations that imply an evolution of exposures that are somewhat different in the U.S. and other parts of the world. Similarly, there appears to be a pattern of exposures, reflected in tissue measurements, that is increasing in recent years (presumably because of the recent introduction of these compounds in new industries). These are important issues and need to be presented more proactively – i.e. in a way that supports or denies these apparent trends in exposure and providing a specific a basis for these observations, if true. As the section now stands, it simply iterates studies in a more or less sequential way, providing some casual notion of the existence of these patterns, but not really determining whether the databases are strong and representative enough to support these conjectures or not. A few specific comments, drawn largely from the BDE-47 document as much of this information is repeated in the subsequent documents, which illustrate the problematic nature of some the discussions that were provided in the document are provided below:

a. There are several places in the discussion of data obtained with 14C that need to be clarified. Either the document poorly explains the nature of the data that is summarized or it has been misinterpreted. One example of a problem in interpretations of greater concentrations of 14C in tissues following a series of doses of non-radiolabeled compound. Such observations are frequently the result of isotope effects (e.g. the prior exposure results in a tissue pool of compound in tissues that is significantly larger than in control animals. As a result more isotope remains in the tissue pools as it becomes diluted in specific activity). The document suggests that these data reflect is a magnification of amounts of chemical that is retained with subsequent doses. This is unlikely. The only way this can be dealt with quantitatively is if the specific activity of the chemical is determined in each tissue for the single dose without prior treatment vs. that observed with a dose after prior treatment with non-labeled chemical.

b. The frequent suggestion that a smaller fraction of dose was absorbed with increasing dose as evidence of saturable absorption may also be inappropriate. There are other possibilities that have to be entertained. In the case of compounds with chemicals of such limited water solubility, such observations may well be explained by limited access to membranes because of low solubility and, more important, the limited solubility in body fluids to carry away the compound from its site of application. The solubilities of these compounds in water are listed as BDE-47 = 11 μg/L, BDE-99 =2.4 μg/L, BDE-209 = <0.1 μg/L, BDE = 0.9 μg/L. The Hughes et al. 2001 study of passage of BDE-209 through mouse skin in vitro would be plagued by this problem unless a perfusion system was used (not stated in the document). Incidentally, the doses applied in this preparation were given in amounts, not concentrations. It is essential to know concentrations to interpret these in vitro studies. The limited solubility could even affect the data obtained with 14C-labeled compounds (e.g. Viberg et al.) because these generally much smaller doses (e.g. 2.2 mg/kg) still exceed the solubility in water by a 4 orders of magnitude in the case of BDE-209. The authors of the papers reviewed may have addressed these issues, but it did not come through in the Toxicological Reviews.

The in vivo studies that employed huge concentrations in the diet would certainly have the same problem. In fact, one wonders whether the lack of clear dose-response in the NTP study of BDE-209 might reflect this problem. Equivalent responses may have been observed at much lower doses. In my view this is a real concern for estimating cancer risk from these data.

3. It is nice to have a reasonably complete discussion of the metabolism of the PDBEs in the IRIS documents. Nevertheless, there is a need to address some confusing aspects of the discussions of uptake, metabolism, distribution, and elimination of compounds in these documents rather than simply reiterating the results. One way of reducing the confusion might be a summary at the beginning of this section that lays out what appears to be happening, even to providing the conclusions of the section up front. This would avoid being surprised by the apparent finding that urinary elimination in mice, for example, appears dependent upon binding of the parent compound to a urinary protein at the end. As the descriptions are laid out, the reader is continuously struck by what appears to be results that appear contrary to general rules (e.g. that non-polar compounds are not efficiently eliminated in the urine).

There are differences among studies related to the apparent extent of metabolism of the compounds and the extent to which metabolites occur in the excreta that are presented without comment. If at all possible, this issue should be driven to conclusions that are useful in making judgments related to how harmful these compounds are. If the information is not useful or conclusions cannot be drawn, this should be stated and the presentation of this material substantially shortened.

Part of the confusion arises from the apparent reliance on measurement of 14C in these studies. These measurements are intermixed with some direct chemical measures, but that is frequently not made clear in the Toxicological Reviews. While these sections read well and are unlikely to be questioned by a casual reader, the informed reader immediately gets distracted by the methodological questions and feels that the apparent conclusions require challenge. Furthermore, questions of metabolism, covalent binding, and distribution are not possible simply by measuring the 14C.

Some specific points in the text of the BDE-47 document are referred to below where the interpretation of ADME data is ambiguous are provided below:

p. 14, 3rd para. This is an example where the legitimacy of the interpretation that there are different amounts absorbed from a dose of radio-labeled compound was administered on day 1 vs. after 10 days of administration of non-labeled compound needs to be questioned.

p. 17, second para in after Metabolism title. The last two sentences appear contradictory.

p. 17, last para. How is "covalently bound" defined (or measured)?

P. 18, 2nd full para. These results for the last day are likely to reflect accumulated metabolites from the prior exposures. Therefore, it is inappropriate to compare the amount of metabolite observed after day 1 to day 10.

p.22, 2nd par. Fifth line. It is not clear where the half-life is being measured. Was it actually in the perirenal fat or was it in the blood? The writing implies that it is in the perirenal fat but the wording is not definitive. This needs to be very clearly stated as most half-life measures are made in blood and that half-life is used to predict turnover in tissues that are sinks (e.g. fat).

Lucio Costa, Ph.D.
Additional comments

BDE-47

p. 9 Discussion on levels in human milk could be expanded.

p. 17 It is unclear why uptake of BDE-47 in cultured neuronal cells in the presence of 10% horse serum "is likely to be more representative of in vivo conditions"

p. 39 It is unclear why data on exposure to BDE-47 in relationship to thyroid hormone levels cannot be used for deriving RfD. The study of Hallgren and Darnerud provides a NOAEL of 6 mg/kg/day and a LOAEL of 18 mg/kg/day. Changes in mixed function oxidase system that were observed at 6 mg/kg/day may be discounted, as suggested.

p. 40 The important issue of pup vs. litter as the statistical unit is discussed, with the indication that the use of more than one pup/litter in the Eriksson et al., 2002 study may bias the results. Yet, in the footnote, a study by Eriksson et al., 2005 (only in abstract form) with BDE-99 is discussed, in which this same issue was shown not to influence the outcome. Perhaps this should be integrated in the main text.

p. 41 An UF of 3 for single vs. chronic exposure may not be necessary. The concept of "windows of susceptibility" during brain development would argue that chronic exposure may not necessarily result in greater adverse effects, but rather that even a single exposure at a specific sensitive time-point may elicit the highest effect. Eriksson et al. have shown with other compounds (e.g. BDE-99) that a single exposure on PND10 is the most sensitive time point. This comment would apply to other BDEs as well.

BDE-99

p. 29 Data on nicotinic receptor changes from the Viberg et al. 2004b study could be presented here. Refer here to data on p. 49.

p. 46 Here and elsewhere, when referring to Casarett and Doull's Toxicology textbook, the most recent edition (2001) could be used.

p. 48 Better references than Klaassen, 1996 or Ankenberg, 2003 could be used to discuss distribution and functions of cholinergic receptors.

p. 48 Discussion of the Ankenberg, 2003 study could be shortened, as it is not of much relevance. It is also presented unclearly.

p. 49 Choose reference other than Klaassen 1996, to indicate effects of atropine. Also, specify % decrease of 3H-QNB binding.

p. 51 Section 4.4.3 (neurotoxicity) should be renamed, as several previous sections (e.g 4.3.1, 4.3.2) already deal with developmental neurotoxicity. Eriksson is also a co-author of the proteomics paper by Alm et al. discussed here.

p. 53 Additional in vitro mechanistic experiments (see references above) may be added here and in section 4.5.3 on mode of action.

p. 56 Data on oxidative stress and BDEs (see references above) may be added here.

p. 57 In section 4.7.2 the reference Branchi et al. 2002 may be added to indicate lack of gender-specific effects.

p. 65 Use of an UF of 3 for extrapolation from subchronic to chronic may not be necessary (see comment for BDE-47). Also, given the availability of several developmental neurotoxicity data on BDE-99, an UF of 10 for database uncertainty seems excessive.

p. 68 The overall confidence in the RfD determined for BDE-99 is listed as low, same as in case of BDE-47. However, given the existence of multiple studies corroborating the main conclusions, confidence level may be raised to moderate.

BDE-153

p. 18 The % decrease of nicotinic receptors in the study by Viberg et al. 2003a could be indicated (see p. 23).

p. 28 UF of 3 for subchronic to chronic may not be necessary (see comments for BDE-47).

BDE-209

p. 12 The possible debromination of BDE-209 to lower bromine congeners may be better discussed, if possible. Should also environmental debromination be mentioned?

p. 16 Half-life may not be necessarily directly linked to rapid metabolism.

p. 38 Content of section 4.5.1 is not in tune with title of section.

p. 58 An UF (e.g. 3) for deficient available database may be added. While, differently from other BDEs, studies are available on subchronic, chronic and developmental toxicity (all yielding NOAELs or BMDs substantially higher than that from the stuies of Viberg et al), no other developmental neurotoxicity evidence is available.

Report is at times repetitive, and could be shortened. For example, results of the Viberg et al. 2003a study are described on p. 10, 33-34, 41-42, 50 and 53.

Ralph Kodell, Ph.D.

Miscellaneous comments

General

The presentation of the data and the derivation of RfDs might benefit from a unified presentation in a single document, instead of four separate documents. In particular, similarities and differences in ADME could be addressed in a cohesive manner.

Specific

BDE-47
Section 3.1, last sentence: It seems that the relative absorption rates of rats and mice are not qualitatively the same in the two studies compared, contrary to what is stated.

Page A-2: The AIC is highest for the selected linear model, which fits best in terms of the p-value. For BDE-209, page A-10, low AIC seems to be one of the selection criteria, along with high p-value. I believe the selection criteria should be consistent. AIC is sometimes used as a weight for averaging the results of several models. It might be a better criterion than p-value.

Page A-2: The indication is that modeling was done for both males and females. But, there were no female data.

BDE-99
Page 81: The Hill model fits best in terms of its having the highest p-value. However, it also has the highest AIC. This isn't consistent with BDE-209, where low AIC is one of the criteria for model selection. AIC should be used consistently.

BDE-209
Page 21: How can 99 mg/kg-day be characterized as a NOAEL in the study by Carlson (1980) when it was associated with a statistically significant increase in the liver-to-body-weight ratio? (Same in Table 2, page 19)

Page 32, lines 5-8: I strongly disagree with the conclusion by Eriksson et al. (2005) regarding litter-based studies. This sentence should be re-stated so that it doesn't sound like this conclusion is accepted as fact by EPA. In general, this conclusion is erroneous.

Page 34, lines 13-15: There is something wrong with the sentence. A decrease in disruption of habituation is not an adverse effect.

Page 38, lines 6-3 from bottom: There is something wrong with this sentence. Thyroid tumors were seen in females as well as males, but they were not significant in either sex. Why is NTP (1984) cited?

Page 39, lines 12-11 from bottom: There is the same problem regarding the statement about thyroid tumio

External Peer Review

Toxicological Reviews for Polybrominated Diphenyl Ethers (PBDEs) Human Health Assessment

FINAL REPORT

Prepared for
Integrated Risk Information System (IRIS) Program
Office of Research and Development
National Center for Environmental Assessment
U.S. Environmental Protection Agency

Prepared by
ORISE IRIS Technical Assistance Team
Oak Ridge Institute for Science and Education
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Toxicological Reviews for Polybrominated Diphenyl Ethers (PBDEs)

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The ORISE IRIS Technical Assistance Team has neither altered nor edited these comments for grammatical or other errors.

Peer Review Project

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The U.S. EPA's National Center for Environmental Assessment (NCEA) has developed several draft Toxicological Reviews for Polybrominated diphenyl ethers. Specifically, toxicological review documents have been developed for tetra-, penta-, hexa-, and decabrominated diphenyl ethers. The charge questions below specifically address the polybrominated diphenyl ethers assessment.

GENERAL QUESTION

Are you aware of other published peer-reviewed toxicological studies not included in these Toxicological Reviews that could be of relevance to the health assessment of BDE-47, BDE-99, BDE-153 or BDE-209?

Ahmed Ahmed, Ph.D.

I have examined the available literature, for the past 10 years, for BDE-47, BDE-99, BDE-153, and BDE-209 by searching under their individual chemical name and chemical abstracts number (CASRN) and crossing the outcome with adverse effects, cancer and/or systemic or genetic toxicity,. I found about 200 citations and their abstracts which represent various types of studies on these compounds. The majority, if not all, of these references are included in various "Toxicological Review" document for one or the other of these chemicals. A detailed literature search analysis is included in this report. The authors of the document may need to verify the existence and use of the appropriate citations in the reviews using the reference manager software programs.

The Toxicological reviews for BDE-47, BDE-99, BDE-153, and BDE-209 are extremely detailed and commonly repetitive. The same information is repeated several times in the same document under different headings (subsection) and in documents for other congeners. Although these repetitions are distracting, I realize they are pluses rather than negatives, I believe that was done to emphasize particular point or effect, to establish the validity of a study and its results and to point out the drawbacks in experimental design or data analysis and interpretation. Therefore, I find the quality of these review documents in a "good to excellent" range. In some of these reviews however, the lack of scientific information makes the decision making processes difficult due to limited number of studies or narrow scientific objectives that disregarded other possible interpretations. This problem does not point to any shortcomings in the efforts of the authors of these documents. Rather it indicates the limitation and shortage of available information (studies).

In a general sense, these chemicals are congeners of each other and because each one is contaminated by one or more of the others. Also, they metabolically, under environmental and biological conditions, are inter-convertible to each other (compounds with higher bromine numbers are converted to compounds with lower bromine). Therefore, I believe that putting them all in one comprehensive review document would serve the purpose more adequately. They almost have the same toxic end points with varying degrees. The effects of these compounds, which came from limited number of studies, are repeatedly compared in each document for each individual compound.

Metabolic and distribution studies are extensively described in the document without deep scientific interpretation of the results nor how these results could be interpreted in the evaluation of human body burden. Furthermore, the purities of the radioactive chemicals used in most studies were not cited. The position of the label as well as the specific activities of the 14C compounds, used in these studies were not indicated in most sections. I am also troubled by the different ways used for the presentation of the doses and concentrations of the compounds and their metabolites in biological tissues (umole, ug, percent of the dose). A unified parameter should be used to insure comparative analysis and easy follow up.

Richard Bull, Ph.D.

I am not aware of other peer-reviewed toxicological studies that would contribute to an understanding of risks associated with these PBDE's. However, some papers included in the review should be better integrated into the derivation of the reference doses.

Lucio Costa, Ph.D.

There are a number of publications that have not been included in the Reviews and that may be relevant to the health assessment of BDEs.
A few studies indicated that house dust is a major source of exposure to BDEs, and for toddlers in particular, dust has been estimated to account for 80% of BDE exposure.

- Jones-Ortazo HA et al., Environ. Sci. Technol. 39: 5121-5130, 2005
- Wilford BH et al., Environ. Sci. Technol. 39: 7027-7035, 2005
- Schecter A et al., J. Toxicol. Environ. Health Part A 68: 501-513, 2005

Contamination of food with BDEs has not been mentioned, yet diet is believed to contribute to the overall body burden of BDEs.

- Hites RA et al., Environ. Sci. Technol. 38: 4945-4949, 2004
- Schecter A et al., Environ. Health Perspect. 114: 1515-1520, 2006

High levels of BDEs were found in children (case study).

- Fischer D et al., Environ. Health Perspect. 114: 1581-1584, 2006

Levels of BDEs were recently determined in plasma of pregnant women in California.

- Bradman A et al., Environ. Health Perspect. 115: 71-74, 2007

Various studies have explored possible mechanisms of action of BDEs, including activation of protein kinase C and induction of oxidative stress.

- Kodavanti PRS, Derr-Yellin EC, Toxicol. Sci. 68: 451-457, 2002
- Kodavanti PRS et al., Toxicol. Sci. 88: 181-192, 2005
- Reistad T, Mariussen E, Toxicol. Sci. 87: 57-65, 2005
- Reistad T et al., Arch. Toxicol. 80 : 785-796, 2006

Ralph Kodell, Ph.D.

I am not aware of any other relevant studies.

1. QUESTIONS RELATED TO THE DERIVATION OF THE REFERENCE DOSE FOR BDE-47, BDE-99, BDE-153 and BDE-209

1.1 Have the rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies been transparently and objectively described in the draft Toxicological Reviews of BDE-47, BDE-99, BDE-153 and BDE-209? Are there additional studies that should be considered for deriving the RfDs for any of the four PBDE congeners?

Ahmed Ahmed, Ph.D.

In all the documents provided, except for BDE-209, no cancer related data was available. In each individual document for every compound there were several sporadic, non cancer related, referenced molecular and systemic toxicological studies. Most of the available and presented studies, unfortunately, toxicological and molecular (receptor binding etc.), were designed to look for the effect(s) of these modern environmental pollutants in light of the toxicological effects of traditional and well studied compounds such as PCB. The large numbers of the reported molecular studies on BDEs were tailored after the effect of poly chlorinated aromatic hydrocarbons. Although the chemicals under review (BDE) are halogenated (brominated) aromatic hydrocarbons, these tailored studies back fired. That is because we ended up with a number of negative or nonspecific effects and obtained limited information to use for the proper evaluation of the risk from BDEs.

The few available systemic toxicological studies are blemished by the fact that most of these studies came from the same laboratory. Although, the data seems to be academically solid, their validity and strength is debatable because it has not been verified in various other laboratories neither in the U.S. nor in other countries. This factor alone weakens but not hinders the derivation of the specific RFD. It makes the confidence in these RFD's low

The authors of the Toxicological Reviews for BDE-47, BDE-99, BDE-153, and BDE-209 have to base their derivation of RFD on continuous scientific information. They used those studies that have specific doses and defined time of exposure as well as a defined adverse effect(s). The only available studies that have dose response and time course were those described by the authors in the texts and were used for the derivation of RFDs. With this in mind, they have clearly and very transparently derived the rational for using these studies. They also took into consideration all drawbacks that weakness each particular study. I was impressed by the way they listed at least 6-10 points explaining their concerns for the use of particular data, in each selected study, in the derivation of RFD for each individual compound. Meanwhile they documented the rational for using the study in their derivation of RFD. There was very clear presentation of the pros and cons of each study utilized in the estimation of RFD.

Richard Bull, Ph.D.

The data available on most of these compounds is quite limited (BDE-209 being somewhat of an exception). In most cases, the risk assessment focuses solely on results from a non-conventional neurodevelopmental test. In one case, BDE-209, a conventional reproductive/developmental toxicity test found no effects at doses much higher than observed in the neurobehavioral study. This may reflect the insensitivity of conventional reproductive/developmental toxicity tests OR more likely, increasingly smaller fractions of the doses being absorbed as doses are increased. The doses utilized were huge, 100, 300 and 1000 mg/kg in corn oil. One would predict that the aqueous phase through which these compounds would have to diffuse to get to an absorptive surface to be exceeded at doses orders of magnitude lower than the lowest dose! Nevertheless, the discrepancies raise significant issues with the standard application of uncertainty factors to results that are clearly more sensitive than conventional methodologies. To put this starkly, either the UFs applied to the "standard" test data are way too small OR smaller UFs need to be applied to these data must be adjusted to account for their much greater sensitivity (and specificity).

There are particular UFs that appear completely inappropriate in the current derivation of reference doses. For example, defaulting to a database uncertainty factor when data of this relative sensitivity to conventional evaluations of reproductive/developmental results are available is very inappropriate.

A more central role also needs to be given to the neurochemical data that is provided, especially those that utilized essentially parallel study designs to the neurobehavioral studies. They are presented as supporting data. They are a lot more than that. They provide an organic measure of modified neural development. It may not be entirely clear how the neurobehavioral and neurochemical data are linked functionally, nevertheless, the two data types contribute as an independent measures that there is an apparently permanent alteration in development. This type of corroborating data should be taken as being much more critical than data from 'standard protocols'. Targeted data of this kind in developmental neurotoxicity would be useful if broadly available. It is simply too expensive and time consuming to identify "critical" endpoints for every compound subjected to safety assessments when the expectation is that such effects are relatively rare. The neurobehavioral data may still be the most appropriate to use for the dose-response assessment, but in a sense the neurochemical data are the critical information. Until I found that data in the documents, I was teetering to the point of saying neurobehavioral data was an inappropriate, unsupported, and poorly understood endpoint (despite what is said in the guidelines).

The more critical question with the apparent developmental impacts of the PBDEs is the apparent consistent developmental neurotoxicity that is seen within this class of compounds. This is observed despite very different patterns of metabolism, distribution, and persistence of these compounds in the body. Some effort should have been expended to see if the relative potency of the PBDEs could be rationalized considering the differences in the extent of metabolism.

On the other hand, one has to be concerned that very similar data have been generated by this same laboratory on a broader set of unrelated compounds. It is time to be concerned about the specificity of these data for developmental neurotoxicity. Independent confirmation is essential when such a apparently non-specific endpoint ends up flagging everything studied.

I most strenuously object to the treatment of these single-dose experiments as being equivalent to a subchronic exposure when applying uncertainty factors to arrive at an RfD. This is justified on the basis that brain development does not occur at an equivalent rate over a lifetime. This question is very relevant to whether of not a body burden approach should have been taken for this endpoint. Scientifically, the question is whether a body burden accumulated over time before the critical period would have the same impact as tissue levels that were achieved by the single dose protocol that was used. The available data do not allow this possibility to be evaluated. Therefore, the assumption that the acute dose at PND 10 is equivalent to a subchronic exposure is highly suspect.

Obviously, the data that are available are not sufficiently developed to allow the development of PK models. However, if evaluated critically (i.e. all the data are not equally informative as indicated in the editorial comments appended to the response to the formal questions) there may be enough absorption, distribution, and elimination data to make some ballpark estimates of consistent measures of how much of the parent compound and/or metabolites are present in tissues. The essential question is whether the effects of 1/10 the dose administered between PND 0 and PND 10 are the same as the full dose that is administered that is administered on PND 10.

This experiment or an analogous one has not been done. Therefore, no conclusions can be made. Until such data are available, these studies have to be treated as a single dose studies, not a subchronic exposure.

There is some serious question related to whether the anti-thyroid effects of these compounds are of importance to the neurodevelopmental effects observed. The data of Zhou et al. (2002) establishes that the antithyroid effects are observed with DE-71, a formulation that might be reasonably linked to neurodevelopmental effects observed with BDE-47 and BDE-99. The Zhou et al. (2002) study was very well done and included not only good dose-response information, but a probable mechanism for the observed effects on thyroid hormone(induced metabolism of thyroid hormone metabolism). As pointed out in more detail in the editorial comments below, the thyroid effects seen in this study occur at doses that are higher than those that produce the neurodevelopmental effects of BDE-47 and BDE-99. As a result, the conclusion needs to be made that the neurodevelopmental effects cannot be linked to the anti-thyroid effects of these compounds.

Lucio Costa, Ph.D.

The rationale and justification for deriving RfDs on the basis of neurobehavioral toxicity studies have been well described and documented. The additional studies indicated above, particularly on body burden in infants and toddlers, would strengthen the health assessments, though they will not change the final determination of RfDs.

Ralph Kodell, Ph.D.

Limited human data do not indicate an association between exposure to PBDEs and adverse health outcomes. However, these data are insufficient to conclude that there is no potential for ~~such effects. For BDE-47, BDE-99 and BDE-153, neurobehavioral effects are the only toxic~~ effects that have been observed consistently in rodent studies of PBDEs, and therefore provide the only data for deriving RfDs. For BDE-209, the NTP rat and mouse bioassays (NTP, 1986) provide suitable data on noncancer endpoints other than neurobehavioral endpoints. The rationale for basing the RfD for BDE-209 on neurobehavioral effects instead of the other effects is that the neurobehavioral effects lead to the lowest point of departure. The rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies is transparent and appears to be objective. I do not know of additional studies that should be considered for any of the PBDEs. However, among the studies that have been considered, I think that greater consideration should be given to some of the studies other than the Eriksson/Viberg studies. Specifically, the studies of Branchi et al. (2002) and Kuriyama et al. (2005) provide data on BDE-99 that is suitable for deriving an RfD. The Branchi data have not been modeled while the Kuriyama data have been modeled but not used.

As noted in the documents, an association between neonatal exposures to BDE-47, BDE-99, BDE-153 or BDE-209 and neurobehavioral dysfunction in humans has not been established. Nevertheless, the behavioral studies appear to provide the most appropriate, dose-response data on adverse noncarcinogenic effects on which to base the health assessment of the four PBDE congeners.

1.2 Do you agree or disagree with EPA basing the health assessment of BDE-47, BDE-99, BDE-153 and BDE-209 to a large extent on the Eriksson/Viberg neurobehavioral studies?

Ahmed Ahmed, Ph.D.

As described earlier, the limitation of the availability of complete and comprehensive one or more studies that evaluate various types of adverse effects of these chemicals necessitated the utilization of what is available such as Eriksson & Virberg neurobehavioral studies. It is well known that there could be no one complete and comprehensive toxicological study. Every individual study will have its own limitation. In spite of some technical weaknesses in these studies, there use in the risk and RFD estimation is warranted.

The reason for the limitation of traditional toxicological evaluation on these newly detected environmental pollutants is because there are no extramural funds in NIH or EPA for this type of studies in the United States of America. That is why we ended up using studies from overseas to set up risk evaluations in the USA. This seems disturbing, specifically if we realize that the concentrations of these chemicals are estimated to be about 10-15 times higher in the biological fluids and tissues of American citizens as compared to European (specifically Swedish) citizens. I urge the responsible agents to encourage the classical toxicological evaluation of these compounds not in light of being similar in their structure to other compounds but in light of the fact that they are highly lipid soluble compounds that form depot in particular tissues of the ecological and mammalian biological systems. These depots create guaranteed life long exposure to these Xenobiotics, even after these chemicals are removed from the environment. The placental storage and transfer (if any) of these chemicals will turn them and their metabolites into trans-generational pollutants.

Richard Bull, Ph.D.

I do support the use of the neurodevelopmental studies for the purpose of deriving points of departure. As intimated above, however, considered alone, these endpoints have too little specificity to be of great concern. There are four fundamental issues: 1) The central importance of parallel neurochemical findings has not been used to advantage (or at least to the advantage it could be), 2) the interpretation of the neurobehavioral data as decreased habituation should be more critically evaluated, 3) the assessments of all the BPDEs depend upon results obtained from a single laboratory, and 4) the overwhelming application of uncertainty factors to such a subtle effect (i.e. relative to the usually accepted protocol) needs to be reconsidered. The first issue was addressed in question 1. The other three are discussed below:

It would have been better to present the actual behavioral data in the document rather than the habituation ratio. This ratio clearly is affected by both the depressed activity seen in the first period and the higher activity seen in the third period. The use of the habituation ratio forces an interpretation that may not be appropriate (or at least the reasons for selecting this parameter was not justified sufficiently in the documents or in the original papers). From the qualitative description of these data that was provided in these documents, they could be interpreted, with equal, if not greater, validity, as a depressed reaction to a novel environment and/or sustained hyperactivity.

Scientific findings need independent confirmation. Thus, EPA should be concerned about placing so much emphasis on set of studies that are generated completely within one laboratory, especially when the methodology and design are peculiar to that laboratory. Although it is not identified in the document, there is corroboration of the findings of Viberg and Eriksson with one compound (PBDE-99) in the study of Kuriyama et al. (2005). The experimental design was somewhat different. Nevertheless, the authors observed an increase in activity at PND 36 with a single dose of 300 μg/kg to the dam on GD 6. The measurement of activity after the animals had habituated to the test system, so the data are comparable to the activity observed in the 40-60 minute interval in the Eriksson et al. (2002) paper. Moreover, the lowest effective dose was somewhat lower than that reported by Eriksson and there is a clear NOAEL at 60 μg/kg.

It must be noted, however, that the implied relationship of the effects of PBDE-99 to altered thyroid function is not substantiated in Kuriyama et al. (2005). The doses producing the neurobehavioral changes occur at too low of a dose to be attributed to changes in thyroid hormone. In general, all the documents need to be more rigorous in their treatment of so-called "mode of action" data.

The application of group of uncertainty factors to a NOAEL despite the fact that the basis of this effect is not established and the apparent subtlety of the response relative to conventional developmental studies is not appropriate. This is discussed in some detail in the answer to question 1.5.

Lucio Costa, Ph.D.

Given the limited body of toxicological information available, use of the Eriksson/Viberg neurobehavioral studies as a basis for the health assessment is the proper approach.

Ralph Kodell, Ph.D.

The study of Eriksson et al. (2001) is the only available toxicity study with dose-response data on adverse (neurobehavioral) effects from exposure to BDE-47. The study of Viberg et al. (2004) ~~has dose-response data on BDE-99. However, the studies of Branchi et al. (2002) and Kuriyama~~ et al. (2005) also provide dose-response data. The data from Kuriyama were modeled and compared to the results from modeling the Viberg data, but the results from the Viberg study were selected for deriving the RfD. The reason for not using Branchi et al. (2002) for modeling is that there is an inversion at the highest dose. This does not seem to be a compelling reason to avoid modeling the data at the other doses. The study of Viberg et al. (2003a) is the only study with dose-response data on adverse effects for BDE-153. For BDE-209, the NTP rat and mouse bioassays (NTP, 1986) provide suitable data on noncancer endpoints as does the neurobehavioral study of Viberg et al. (2003b). Data from these studies have been evaluated and compared. There seems to be no alternative to basing the health assessment of the four PBDEs to a large extent on the Eriksson/Viberg studies, but the additional modeling for BDE-99 should be done and compared to Viberg (2004).

1.3 Are the Eriksson et al., 2001 (BDE-47), Viberg et al., 2004 (BDE-99), Viberg et al.,2003a (BDE-153) and the Viberg et al., 2003b (BDE-209) studies appropriate for determining the point of departure? Have the strengths and weaknesses of the Viberg and Eriksson studies been appropriately characterized and considered?

Ahmed Ahmed, Ph.D.

Following my review of the original reports, I found that Eriksson et al, 2001 (BDE 47), Virberg et al, 2004 (BDE-99), Virberg et al., 2003 (BDE-153) and Virberg et al, 2003b, 2003 (BDE-209) represent the most relatively complete studies on dose/response (neurobehavioral effects) relationships in animals. Most other available studies, discussed in these documents, could not directly correlate or tie the dose response and time course relationships. My main concern is that all these studies are coming from one group of scientists who pioneered the neurobehavioral / ADME (distribution in rodents) evaluation of these chemicals. With this information, come the problems of lack of validation of data coming from one laboratory with other data coming form other laboratories on the same scientific issues. Nevertheless, the authors of these reviews have clearly and transparently judged these studies without biased. They expressed the weakness of each study as well as its strengths in their utilization for driving the RFDs. The authors should be commended on their unbiased evaluation.

Richard Bull, Ph.D.

It is my opinion that these data are appropriate as long as it is emphasized that the neurochemical data that have been collected using parallel protocols add significant support to the conclusion that a modification(s) of the normal developmental pattern occurs as a result of these treatments. Please note that other neurobehavioral data were identified in the PBDE-99 document that should have been more formally considered as indicated in the response to question 1.2. Moreover, the data sets on activity per se are much more appropriate for dose-response assessment than the habituation ratio, for reasons provided above. The habituation ratio is derived data, but the data provide very little support for the idea that loss of habituation is the basis of these results.

Lucio Costa, Ph.D.

The studies by Eriksson and Viberg are unusual, as indicated in the reports, but are the only available for most BDEs. At this stage, they are the only ones available for determination of point of departure. However, the study of Kuriyama et al. (2005) should be considered for determination of point of departure for BDE-99. Strengths and weakness of these studies have been described appropriately (but see comments below). A sentence may be added to indicate that further developmental neurotoxicity studies are needed for BDEs.

Ralph Kodell, Ph.D.

The Eriksson et al. (2001) study appears to be the only study available with data that might be used to determine the point of departure for BDE-47. For BDE-99, data from several candidate studies are modeled for determining a point of departure. The Viberg et al. (2004) study appears to have the best dose-response data and to provide the best model fits. However, the data from Kuriyama et al. (2005) also fits acceptably and gives lower BMDLs for some endpoints. Reasons were given for choosing the Viberg-derived BMD over the Kuriyama-derived BMD, but I think the Kuriyama-derived value is equally justifiable. The only well-designed dose-response study with dosing both pre-natally and post-natally (Branchi et al., 2002) was not modeled because of an inversion at the highest dose. Conceivably, these data could be modeled for BMD estimation, perhaps by omitting the highest dose, as is sometimes done with cancer incidence data. The Viberg et al. (2003a) study is the only study with dose-response data for determining a point of departure for BDE-153. Both the NTP bioassay in rats and mice (NTP, 1986) and the study of Viberg et al. (2003b) in mice provide data appropriate for determining a point of departure for BDE-209. Of these, the Viberg et al. (2003b) study gives the lowest point of departure, and is thus selected.

A clear weakness of the Eriksson/Viberg studies is that they did not conform to health effects test guidelines for a neurotoxicity screening battery or developmental toxicity studies. The dosing regimen did not include gestation and lactation exposure, and only single doses were administered. More than one pup per litter was used for behavioral testing, thus confounding dose effects with litter effects. (Although the authors reported doing a split-plot analysis of variance in all four primary papers, which would correctly recognize and use the litter as the experimental unit for testing treatment effects, their pair-wise testing for such effects appears to have treated each pup as an independent experimental unit.) In the cases of BDE-153 and BDE-209, the dose-response data were not considered suitable for statistical modeling because only graphical information was available. These weaknesses have been characterized and considered, and offsetting strengths have been discussed. However, it is surprising that the data on BDE-153 and BDE-209 cannot be recovered from the authors to allow dose-response modeling and BMD estimation. One important weakness that was not emphasized for BDE-47, BDE-153 and BDE-209 is that the Eriksson/Viberg mouse studies were done in males only.

1.4 Have the most appropriate critical effect and point of departure been selected? And has the rationale for the point of departure been transparently and objectively described?

Ahmed Ahmed, Ph.D.

With all the above consideration the authors have critically and objectively selected the most critical effect (neurobehavioral) and established the most appropriate point of departure (dose response) for all chemicals under review. The authors have very clearly rationalized, in great detail, in each individual review, their selection of each particular point of departures.

Richard Bull, Ph.D.

Among the data that are available, the neurobehavioral data provide the best data for identifying a point of departure. There are some lingering questions that relate to effects of BDE-99 that are reflected in histologic changes that occurred in the ovaries and vaginal epithelium at very small doses (i.e. 0.06 mg/kg day). However, these data were not described with sufficient clarity in the document to determine if they should not be used (i.e. neither incidence or severity are described in the context of dose-response).

My review of the Talness et al. (2005) study does raise some issues both about design and interpretation that may have been the basis of the Agency's apparent reluctance to use the Kuriyama et al. (2005) data on PBDE-99 (although it was not stated, if that were the case). For example, it is difficult to understand the conclusion that necrosis was observed by electron microscopy (Fig 1 & 4), but were not observable by light microscopy (see p. 194, section 3.1.2). Second, the number of animals examined for changes in the vagina was very small. Further, the authors do not make clear the basis for their repeated assertion that the doses tested resulted in levels of 6-29 times greater than reported in human breast adipose tissue. Was a human study conducted that looked at single doses that gave rise to such levels? I could find no reference to such a study.

Lucio Costa, Ph.D.

The most appropriate critical effect and point of departure have been selected and the rationale has been adequately described.

Ralph Kodell, Ph.D.

Although the seriousness of decreased habituation capability as a manifestation of an adverse effect on spontaneous motor behavior is not discussed, it is a common measure of developmental toxicity across studies. Thus, it appears to be an appropriate critical effect for deriving a point of departure. However, the individual measures of decreased habituation might be as appropriate as or more appropriate than the habituation-ratio as indicators of toxicity. For BDE-153 it is unfortunate that data on neither the habituation-ratio nor the swim-maze learning/memory test could be recovered for modeling. The dose-response for the swim-maze effect might be different from the habituation-ratio dose-response. (Unfortunately, swim maze data on BDE-99 (Eriksson et al., 2001) involved only a single high dose.) For BDE-209, too, it is unfortunate that dose-response data on the habituation ratio cannot be recovered for modeling and BMDL calculation. It's not clear why the actual data on BDE-153 and BDE-209 cannot be recovered from the studies' authors, given that the studies were published fairly recently (2003). In fact, it would be good if the dose-response data for all four PBDEs could be obtained so that litter effects could be handled properly in the BMD modeling. It would be far better if a BMDL rather than a NOAEL for habituation-ratio could be used for setting an RfD for neurobehavioral effects of BDE-153 and BDE-209.

For BDE-47 and BDE-99 and BDE-209, the rationale for selecting the point of departure in terms of the BMD and associated BMR are clearly spelled out. Selecting the BMD as the dose that corresponds to a shift of 1 standard deviation in the mean (BDE-47 and BDE-99) corresponds approximately to a 10% BMD with a critical cut-off defined by assuming 1% background risk for a normal distribution with constant variance. The use of a BMR of 10% for the BDE-209 quantal noncancer endpoints is explained. I think it ought to be stated explicitly that the BMDL rather than the BMD is used for these endpoints in order to account for experimental uncertainty (variation), which is a good practice and is related to the use of uncertainty factors. (However, the uncertainty may be understated because of treating littermates as independent experimental units.) Generally, for each endpoint, the BMD and BMDL resulting from the best-fitting model (or an average of the best-fitting models: BDE-209) and/or the model fitted to the most dose groups are selected. Then, the lowest BMDL among those is selected as the point of departure. The sequential likelihood-ratio testing approach for selecting the fitted model for neurobehavioral effects of BDE-47 and BDE-99 is very sound and is explained very clearly. However, I do not understand why, in the case of BDE-99, it must be assumed that 8 animals of each sex were tested behaviorally. Can't this be clarified by contacting the study's authors?

To the extent that data are available for dose-response modeling, I believe that the selection of critical effects and points of departure are appropriate, and that the rationale for the points of departure has been transparently and objectively described. However, I think a strong effort should be made to recover neurobehavioral toxicity data from the authors (Viberg et al., 2003a, 2003b) to allow dose-response modeling and BMD/BMDL calculations for neurobehavioral effects of BDE-153 and BDE-209, and to refine the modeling for BMD-47 and BMD-99.

1.5 Have the rationale and justification for each uncertainty factor (UF) selected in the draft Toxicological Reviews of BDE-47, BDE-99, BDE-153 and BDE-209 been transparently described? If the selected UFs are not appropriate, what alternative UFs would you suggest and what are the scientific rationales for those suggested? Does the database support the determinations of the RfDs for BDE-47, BDE-99, BDE-153, and BDE-209?

Ahmed Ahmed, Ph.D.

In their calculation of each individual RFD for each PBDPE, the authors have clearly classified several uncertainty factors for each compound based on the available information in the studies utilized. I found that their selection of these uncertainty factors to be well rationalized and the objectivity of each uncertainty factor to be very clear. It was apparent that the number assignment was very uncertain during the panel meeting on Feb 22,2007. It seemed very uncertain whether several UFs should be assigned a10 or 3.

In considering acute versus chronic uncertainty factor, I feel that the accumulation of BDEs, specifically the lower brominated compounds, tetra (BDE-47 and penta (BDE-99) should be considered in the calculation of their RFDs. These compounds detected in various human tissues and biological fluids and have very long half lives in human tissues; the adipose tissues in vital organs and biological fluids; breast milk. Thus, for the highly susceptible human groups such as fetuses and infants there will be continuous internal dosing that is coming from storage depots. Accordingly, the body burden for infants will not be only dependant on exposure to external dosing from the environment. It will be dependant on a combination of external (environmental) and internal factors (the depot of biological tissues and fluids). This complexity should be considered in the estimation of RFDs. Specifically for the U.S. population. In the American population, the levels of most of these chemicals in blood, tissues and biological fluids are about 10 or more times higher than that detected in biological fluids from other (European) countries. Such facts should be considered in the calculation of RFDs here in U.S.A. Finally I believe that available limited data base should support the determination of the RFDs for BDE 47, BDE 99, BDE 153, and BDE 209.

Richard Bull, Ph.D.

The rational and justification of each UF has been transparently described. However, I believe that they have been inappropriately applied to these chemicals.

There was no consideration in the document related to the specificity and sensitivity of the neurobehavioral and neurochemical measures that have been applied vs. more standard endpoints. In particular, it is inappropriate to apply the UF relative to data base inadequacies. One might consider modifying UFA and UFH as well.

Given the nature of the available data, the rationale for using an adjustment from subchronic to chronic exposures (UFS) for these data is also not sustainable scientifically. In this case, the critical issue is whether the body burden of parent compound is important. Thus, the adjustment of 3 that is made on the UFS is not appropriate. Rather one needs to consider the extent to which the mother's pre-pregnancy accumulated body burden would influence the developmental outcome. As I see no way of even making a judgment on this issue based on the available data, I suggest that UFS be raised to 10.

There is a more general problem with the database uncertainty factor when it is applied to the development of RfDs. The traditional across species and within species uncertainty factors relate to the critical endpoint being addressed in the risk assessment. The database uncertainty factor addresses questions that go beyond this endpoint and focus on risks that might occur, but there are no relevant data. Thus, it does not reflect on the accuracy of the assessment of the endpoint being evaluated. This uncertainty factor is more appropriately applied at the point that risk management decisions are being made (e.g. at the point that MCLs are being developed). This concern should be introduced at the point where other parallel uncertainties are entertained (e.g. can remediation efforts reduce the risk or whether the MCL is within a range that can be measured).

Lucio Costa, Ph.D.

The selection of UFs has been described in detail, though I do not fully agree with some choices (see comments below for individual BDEs). The database on which RfDs are determined is in most cases very poor, particularly in case of BDE-47 and BDE-209. Perhaps RfDs should be acknowledged as "temporary", while waiting for additional studies that may increase confidence.

Ralph Kodell, Ph.D.

Default uncertainty factors of 10 for UFA and UFH are used for BDE-47, BDE-99 and BDE-153 without much explanation or justification. For BDE-209, the UFA default (but not the UFH default) has been explained satisfactorily. Taken together as a product, values of 10 each for UFA and UFH may be overprotective, but there is no alternative methodology that is currently accepted for expressing these factors as a smaller unitary factor, as might eventually be done via hierarchical modeling.

Looking at these factors separately, a UFA of 10 might at first seem conservatively large given that no evidence of an association between neonatal exposure to PBDEs and neurobehavioral effects in humans exists. On the other hand, there is no evidence to the contrary, and the mode of action is not yet understood. Because the potential adversity to humans is present, a value of 10 seems justifiable in all four cases. For UFH, I believe there is justification for deviating from the default value for all four congeners. Because the neurobehavioral effects seen in rodent studies result from exposures at critical points in early development, I believe it can be argued that the most sensitive members of the population for these effects (neonates) are already accounted for. Because the default value of 10 is used to account for differences in sensitivity among all members of a population, and because it seems hard to justify a factor that large for variation just among neonates, a smaller value of UFH appears justified. I recommend a value of 3 for UFH for all four PBDEs.

The choice of 3 for UFS for all four congeners appears justifiable to me, recognizing that timing of exposure is more critical than duration of exposure for the neurobehavioral effects observed. However, I regard this factor as accounting more for uncertainty arising from a lack of pre-natal exposure in the studies used to derive the RfDs than for uncertainty regarding potential effects of chronic exposure.

Using a value of 10 for UFD for BDE-47, BDE-99 and BDE-153 does not seem justifiable. In my opinion, if the database is so uncertain as to require a UFD value of 10, then the database is too limited to allow the derivation of meaningful RfDs. The primary neurobehavioral endpoint appears to be quite sensitive, and it is consistent across congeners. For BDE-47, I recommend a UFD value of 1. Although there is only a single study, the neurobehavioral endpoint is the same as for the other congeners, and dose-response data are available for basing the point of departure on a BMDL. For BDE-99, I also recommend a UFD value of 1. There are several studies and dose-response data are available for basing the point of departure on a BMDL. For BDE-153, I recommend a UFD value of 3. There is only a single study, and dose-response data could not be recovered for BMDL calculation. If those data can be obtained from the study's authors and used for BMDL calculation, then this factor could be reduced to 1. For BDE-209, I recommend raising the factor from 1 to 3. Granted, there are data from more than one study, and BMD modeling was done along with model averaging for non-neurobehavioral effects. However, a NOAEL for neurobehavioral effects rather than a BMDL was selected for the point of departure, because of the inability to recover the neurobehavioral dose-response data. To me, the absence of definitive data for dose-response modeling for neurobehavioral effects reflects an inadequacy in the database, and in fact, inadequacy in the very data ultimately used for deriving the RfD. If data can be obtained from the study's authors and used for BMDL calculation, then this factor could be reduced to 1.

One factor that is not mentioned is UFL for going from a LOAEL to a NOAEL, because LOAEL-to-NOAEL extrapolation is not done here. However, I think this factor should also apply when using a BMDL10 as a point of departure. A 10 % benchmark response is not negligible. A BMD10 (BMDL10) is more in line with a LOAEL than with a NOAEL. I recommend applying a UFL factor of 3 to each of the BMDL10 values to account for uncertainty in extrapolating from a dose of non-negligible toxicity to a dose of negligible toxicity.

I believe the database supports the determinations of RfDs, but I agree with the statements in the documents that the overall confidence in the RfD assessment of BDE-47, BDE-99 and BDE-153 are low. I feel the same way about BDE-209.

2. BODY BURDEN APPROACH

2.1 Are there adequate data for considering body burden as an alternative dose metric to administered doses in any of the RfD derivations?

Ahmed Ahmed, Ph.D.

The current available animal and human data regarding the body burden of BDE's are sporadically designed and extremely limited. Although there are several studies under each compound that describe the ADME or body burden concept (absorption, distribution and tissue accumulation and excretion), the kinetics (t1/2, volume of distribution, rates of absorption, metabolism and excretion) of the absorption, accumulation and removal processes of each individual compound have not been established. Similarly the identity, type and structure of the accumulated chemical species have not been recognized. In natural environmental exposure setups, there is no single (exposure) dose. Humans are continuously exposed, continuously storing, distributing, metabolizing and excreting the compounds or their metabolites. In this regard even the year or more long half life, described for some congeners, is in reality not a true kinetic factor, because the parent molecules or its metabolites are primarily stored in certain target tissues and continuously released into the blood for circulation, metabolism and excretion. These tissue stores are continuously replenished by absorbing more from the external surrounding environment. All these events should be taken when considering body burden as an alternative dose metric in the derivation of any of the RFDs. Such information is currently scarce (McDonald, 2005).

Richard Bull, Ph.D.

There may be a reason for considering body burden. As indicated in the response to questions 1.1 and 1.5, the question of whether increased body burden would contribute to the critical neurobehavioral endpoints evaluated has simply not been tested. It is for this reason that treating a single dose experiment as if it were a subchronic exposure is inappropriate. In addition, it is not clear whether the body burden or daily dose is the best dose metric for the chronic effects of those members of the PBDE class that have been evaluated in chronic studies. Therefore, this question also depends upon the endpoint that is being evaluated and the documents have not provided a basis for either approach. There are huge inconsistencies in the ADME among the PBDEs. Chronic exposure would appear to lead to large body burdens with some of the PBDEs, but not others. Furthermore, simply showing that the compound, a metabolite, or a radiolabel derived from that compound reaches its target site does not establish a causal link. For the developmental effects, in particular, the question of whether levels of the parent compound or a metabolite is the most appropriate dosimeter has to be resolved experimentally, not guessed at. As a start, the variability in the extent of metabolism across these four PBDEs needs to be evaluated to see whether the neurodevelopmental effects appear to occur at similar body burdens of the parent compounds. That is about as far as an analysis could be taken given the data that are available.

The above points are critical as the only compound for which there are cancer data is BDE-209, which appears to be metabolized and excreted much more rapidly than the PBDE's with lower bromine substitution. It does not bioaccumulate to the extent of the other compounds. Therefore, even this chronic effect may not be a function of the body burden. Part of this may have resulted from the lack of context provided for the metabolism & kinetic data that were provided. There are several aspects of the write-ups that suggest that data to this effect may exist, but were simply not critically and/or creatively interpreted or used by the authors of the document. Some of these issues are discussed in greater detail in the editorial comments provided below. To make proper use of the available metabolism and kinetic data that are available requires an integrated assessment of all four compounds. Therefore, one questions why these chemicals are addressed in four separate documents.

Lucio Costa, Ph.D.

Body burden would be an alternative dose metric to derive RfDs, however, current available data are still too limited, in my opinion.

Ralph Kodell, Ph.D.

There are not adequate data for considering body burden as an alternative dose metric to administered dose.

2.2 Do you agree with the rationale described in the Toxicological Review of BDE-99 that the data on the window of susceptibility of the cholinergic receptors to BDE-99 tend to minimize body burden concerns?

Ahmed Ahmed, Ph.D.

Even though I don't completely agree and don't understand clearly the question, I have to accept the concept. That is because any experimental design has to have an assumption that is based on the available information. We know from the literature that the fetal and neonatal brain developments are different in rodents and humans. Therefore, fetal and neonatal cholinergic receptors regulation (up or down) could also be different. While brain development in rodents occurs during postnatal periods, it occurs in utero in humans. Both conditions have extremely different manifestations regarding nutritional, environmental exposure and other toxicokinetic parameters. Therefore, to focus on a specific and certain particular time for susceptibly (PND 3, 7 or 10) for cholinergic receptors in neonates may increase the uncertainty factor in the RFDs' calculation.

Richard Bull, Ph.D.

I am not sure that I understand this question. There is no direct evidence provided that BDE-99 treatment directly affected cholinergic receptors that I could identify in the document. What was presented was an indication that animals treated neonatally with nicotine were responsive to the "loss of habituation" following dosing with BDE-99 at 8 mg/kg at 5 months of age. The effect was not produced by nicotine pretreatment alone, or by only administering BDE-99 at 5 months of age. This is not evidence of an interaction at cholinergic receptors! On the surface, the data obtained with preadministration of nicotine appears to actually separate the mechanism of nicotine from that of BDE-99. The nicotine effects are actually inverted (i.e. suppressed activity) with nicotine at higher doses. Why do neither BDE-99 or nicotine, administered alone, produce the effect when administered at 5 months? The mechanism of the interaction must be complex and indirect.

The second part of the story is that nicotine treatment at PND 10 caused decreases in binding sites for bungarotoxin and QNB, that specifically bind to nicotinic and muscarinic subtypes. A similar effect was observed with BDE-99 administered at PND 10. It is unlikely that the effects of BDE-99 are an expression of an interaction at nicotinic receptors, per se. Binding to such receptors has structural requirements not remotely met by BDE-99 or any of its likely metabolites. Whatever BDE-99 does must involve a less direct mechanism. That could be an inhibition of the expression of these receptors, but just as likely, it could mean that there is a deficit of neurons that express these receptors. If the document goes into mode of action questions, it is imperative that it clearly distinguishes among alternative mechanisms that are possible. One of those criteria clearly has to be a consistency in the doses required to produce the effect and that needed to activate a particular mechanism thought to be a key event in the mode of action. If one mechanism is considered to be more probable, the reasons for this conclusion need to be explicitly stated. Otherwise the document has to conclude that the mechanism of these effects have not been established.

Lucio Costa, Ph.D.

Question is unclear.

Ralph Kodell, Ph.D.

The hypothesis of impaired development of the cholinergic system during the postnatal "brain growth spurt" period as an explanation of the neurobehavioral effects seen in the Eriksson/Viberg studies is plausible. Staskal et al. (2006b) showed that brain levels of BDE-47 administered to neonatal mice on PND 10 were higher than levels in adult animals. Branchi et al. (2002) showed significantly elevated brain levels of BDE-99 in mice administered a high dose from GD 6 to PND 21. Eriksson et al. (2002) also showed that radiolabeled BDE-99 can be taken up and retained in the neonatal mouse brain, although the amount of radioactivity in the brain was only between 0.4% and 0.5% of the administered dose. Viberg et al. (2003b) reported a similar result for BDE-209. The limited data available on BDE-99 indicate that the effects on habituation were seen only at doses that also cause decreased binding of the cholinergic receptor antagonists. For BDE-153, Viberg et al. (2003a) showed that the density of nicotinic acetylcholine receptors in the hippocampus of 6-month old mice treated on PND 10 was significantly decreased at 9.0 mg/kg, a dose at which mice showed significant defects in learning and memory. However, there are no definitive data on mode-of-action. PBDEs have some structural similarity to the thyroid hormone T4. It has been suggested that they may interfere with thyroid hormone transport by competitively binding with one of the transport proteins in plasma. Although it is known that thyroid hormones are essential for normal brain development in humans and that decreases in thyroid hormone levels during fetal and early neonatal life may have profound adverse effects on the developing brain, thyroid hormone levels and behavioral activity were not co-measured in any of the developmental toxicity studies in mice or rats. Although the data on the window of susceptibility of the cholinergic receptors to the PBDEs (PND 3 – PND 10) are suggestive, I believe there are too many other possibilities for mode of action for this rationale to minimize body-burden concerns.

3. QUESTIONS RELATED TO THE CARCINOGENICITY ASSESSMENT OF BDE-209

3.1 Is the weight of evidence for the carcinogenicity of BDE-209 in the draft Toxicological Review appropriately described? Are there additional studies that should be included?

Ahmed Ahmed, Ph.D.

The weight of evidence on the carcinogenicity of BDE 209 in the draft toxicological review is based on a carcinogenicity studies that were conducted more that quarter of a century ago. Although the authors of the draft review document have provide a methodical and complete description of the studies, the study itself and its results leave a lot to be desired. Modern, molecular and more sensitive biomarkers of cancer should be implemented in future carcinogenesis studies for BDE-209 and other congeners. The current available studies had shed some doubts regarding the pre-carcinogenic effects of BDE 209. The studies utilized very high doses which lead to some toxic effects and increased animal deaths.

Currently I am not aware of any recent study that addressed the carcinogenicity of BDE-209.

Richard Bull, Ph.D.

Yes.

Lucio Costa, Ph.D.

The weight of evidence for carcinogenicity of BDE-209 is appropriately described. I am not aware of any additional studies.

Ralph Kodell, Ph.D.

The weight of evidence for the carcinogenicity of BDE-209 is appropriately described. I do not know of additional studies that should be included.

3.2 Do the data support estimation of a cancer slope factor for BDE-209? If yes, is the rationale for the quantitative analysis objectively and transparently described, considering the uncertainty in the data and the suggestive nature of the weight of evidence? Have the rationale and justification for the use of linear low-dose extrapolation been objectively and transparently presented?

Ahmed Ahmed, Ph.D.

The available data supports the estimation of a cancer slope factor for BDE-209. The rationale for the qualitative analysis was objectively and transparently described. Similarly the justifications for the use of linear low dose extrapolation have been objectively presented.

Richard Bull, Ph.D.

After reading the public comments directed at treatment of the carcinogenesis data that is available on BDE-209, it is apparent that there are a variety of problems with the NTP data. Comments from industry focused on the fact that the responses were fairly modest and that the criteria have changed for classifying liver lesions in the rat since this study was completed. I am less concerned with the scoring nodules as tumors. Nodules generated in initiation promotion protocols are known to regress with suspension of treatment. This is much less likely to happen with chronic studies of a single compound.

However, I question the appropriateness of the original NTP study for developing risk estimates in general. The very high concentrations were provided to the animals in the diet make it almost certain that the external dose is not a reliable indication of the systemic dose. The extremely low solubility of BDE-209 in aqueous media (<0.1 ug/L) suggests that the transfer rate from food to aqueous phase would sharply limit to absorption proportional to external dose to much lower concentrations than the 25,000 and 25,000 ppm in the diets used in the NTP study. The document contains data indicating that absorption is sharply curtailed at much lower concentrations in the diet (see quotation of studies of El Dareer et al., 1987) and the fact that much higher percentages of absorption were derived from the gavage dosing of much smaller doses of PBDE-209 (see Sandholm et al. 2003; Morck et al. 2003). These observations are supported by the more uncertain studies of the absorption of the labeled compound. While there were some evidence of tumor induction in both mouse and rat studies, there was little indication of dose-response, suggesting that the response was limited by absorption. If this is the case, the true point of departure for estimating cancer risk could be order of magnitude lower than is suggested by the doses administered. For this reason, revisiting the results of the NTP studies will be a waste of time and money. I would strongly suggest that a new bioassay be conducted that can be more easily related to environmental exposures. The doses administered in such studies should be established based on better designed studies of absorption, distribution and metabolism than have been conducted to date and development of a first generation PBPK model.

Lucio Costa, Ph.D.

Data are indeed suggestive of a carcinogenic potential of BDE-209. BDE-209 does not appear to be genotoxic (though database is limited), but no clear indication of possible epigenetic mechanism is available. On the other hand, chronic toxicity studies suggest the induction of non neoplastic or pre-neoplastic lesions in target organs. The linear low dose extrapolation as a default, conservative approach appears justified in this case, as is the classification of BDE-209 as a possible human carcinogen.

Ralph Kodell, Ph.D.

The data appear to support estimation of a cancer slope factor for BDE-209 based on neoplastic nodules or carcinomas (combined) in the livers of male rats (NTP, 1986). This conclusion assumes that any change in the classification of neoplastic nodules that might have taken place subsequently would not change the dose-response appreciably. The rationale for the quantitative analysis is transparently described. The cancer data are characterized as providing "suggestive evidence of carcinogenic potential," in keeping with the EPA cancer guidelines (EPA, 2005a). The modeling of several tumorigenic endpoints leads to selection of the cancer slope factor corresponding to the most sensitive endpoint (liver nodules/carcinomas). I did not see a rationale or justification for the use of linear low-dose extrapolation, except for a reference (page 62) to two EPA guidelines documents for cancer assessment (EPA, 2005a, 2005b).

3.3 Are there alternative modeling approaches that should have been considered instead of or in addition to the linear low-dose extrapolation approach?

Ahmed Ahmed, Ph.D.

To my knowledge the authors have explained all possible modeling approaches. They selected the best fit model for their interpretation of the experimental data. I commend the authors' consciousness for siting the drawbacks of these studies and for the thorough analysis of the available data.

Richard Bull, Ph.D.

There are no data that would permit departure from linear low-dose extrapolation. As indicated above, I am concerned about the very high doses that were used in these studies. It is not clear that absorption would be linear with dose because of the solubility problems that are discussed in more detail in the editorial comments that have been appended to these responses to EPA's specific questions.

Lucio Costa, Ph.D.

Data are indeed suggestive of a carcinogenic potential of BDE-209. BDE-209 does not appear to be genotoxic (though database is limited), but no clear indication of possible epigenetic mechanism is available. On the other hand, chronic toxicity studies suggest the induction of non neoplastic or pre-neoplastic lesions in target organs. The linear low dose extrapolation as a default, conservative approach appears justified in this case, as is the classification of BDE-209 as a possible human carcinogen.

Ralph Kodell, Ph.D.

Other modeling approaches could have been considered, but I don't think that they necessarily should have been considered. The liver dose-response data are quite linear and there are only two nonzero doses plus a zero-dose control. The linear model fits quite well. It seems likely that other dose-response models would give similar fits. It's possible that such models would extrapolate differently from the linear model below the data, but it is my opinion that the data themselves are not informative enough to justify a different, say, sub-linear, extrapolation approach.

MISCELLANEOUS REVIEWER COMMENTS

Ahmed Ahmed, Ph.D.

Comments on Each Document:

BDE 47:

1. Page 7; 3.2.1: Current Human data regarding distribution and disposition of BDE 47 is spotty, sporadic with low number of samples and uncontrolled health and environmental conditions, with no regard to geographical or ecological circumstances.

2. Human data should be summarized and presented in a comprehensive table with references in this and in all other documents.

3. Page 13; 3.2.2: Animal data on the disposition of BDE-47 focused on several 14C labeled compounds. In most of these studies, the position of the label was not mentioned, the purity of the 14C-compound was not known, the specific activity of the compound was not given and the ADME studies were based on following the radioactivity in various tissues and biological media. No pharmacokinetic parameters were estimated from these studies.

4. The identity of the detected radio labeled species in tissues and biological fluids is very important to clarify whether this species is the parent molecule, a metabolite or even a carbon dioxide molecule.

5. The levels of radioactivity should be uniformly expressed throughout this document and other documents. That is essential to be able to do reasonable comparisons among various congeners. Concentrations as mg-equivalent / g tissue/g lipid weight should be used across the document.

6. I suggest that the authors to put some proposed metabolic pathways for this compound. It could be extracted from other brominated congeners such as BDE-99. The proposed metabolic pathway similar to that presented for BDE-99 could be used here too. This will strengthen the fact that this and other lower brominated congeners could be obtained from higher brominated ones.

Mice are known to have higher levels of various CYT P450 enzyme activities than rats. This should be reflected in the discussion of the differences in the disposition, metabolism and excretion of this compound and other congeners.

8. Extensive explanation of receptor site interaction is somewhat confusing due to the lackluster effects of these compounds on various receptors. It would be beneficial if a summary table is presented either in the beginning or at the end of this section. Relative potency of various congeners on specific receptors should be indicated.

9. A table, in page 39, that could summarize the neurobehavioral, developmental and reproductive effects of BDE-47 should be added. It will show how Eriksson et al represent as complete a study to be used in RFD determination. It will be helpful if in each document a similar table is inserted before the selection of the principal study as in case of the document of BDE-99.

10. The Uncertainty Factors for population at risk (fetuses and newborn) and for conversion from single dose to multiple and continuous routes of exposure should be adjusted for, as described before.

11. The neurobehavioral studies that are utilized in RFD evaluation have limited end points and were conducted in one Swedish research location. Due to the lack of complete dose response/ time course studies, I have to agree on using them in the determination of the corresponding RFD. My agreement is based on the fact that these studies have statistically significant end points for neurobehavioral adverse effects within the framework of the experimental design.

12. A major concern about the experimental design, described in these studies, is ignoring the "letter effect". The authors of the study should have used offspring from multiple letters rather than from one letter. Randomization was based on only two letter and randomization approach was not described.

13. Although radioactivity was detected in brain, in the studies, there was no explanation in which brain areas radio activity was detected. Anatomical or histological localization of the radioactivity would have added significant weight to the mechanisms of the observed neurobehavioral studies.

14. There seems to be no correlation between the postnatal day of exposure and the concentration in the brain. Exposure at PN Day 10 provided the brain with the highest concentration while had no increase in neurobehavioral adverse effect.

BDE-99

1. The table in page 58 is an excellent summary to the developmental and reproductive effects of several BDEs. It shows how Viberg et al (2004a) represent as complete a study to be used in RFD determination. It will be helpful if in each document a similar table is inserted before the selection of the principal study for RFD estimation.

2. Study of Kuriyama et al (2005) showed some good dose-response relationship for neurobehavioral as well as male reproductive effects. This study should be considered in the determination of RFD for BDE-99.

3. ADME evaluations in animals are un-objectively presented. They were presented as several summaries of several studies but with no connection and with limited interpretations of the data. The proposed metabolic pathway presented in page19 is very helpful. Similar pathway should be presented for other congeners.

4. Due to the metabolic relationship between higher and lower congeners of BDE, a comprehensive metabolic profile for all of these compounds should be presented in every toxicological review for each individual BDE.

5. Comments on the radioactive compound, its purity and specific activity that are described before, will also apply for this and every other congener.

6. There are large number of receptor studies that are presented in the document. A comparative summary with references will be helpful for the reader to easily conclude which is the most sensitive receptor for this and other congeners.

7. Concerns regarding Uncertainty Factors described before, apply here, too, for BDE-99.

BDE-153

1. Human distribution studies are somewhat sporadic and most of them were designed for the detection of other chemicals. The data in table 5 should be expanded to include BDE- 209. This table should be presented in the document of every congener.

2. I would suggest that the authors of the document should create a summary of values for the concentration of various PBDs in human tissues in various geographic locations. Schecter et al (2003) showed that the mean median concentrations of BDE in Texas are much higher than any other places in USA or Europe.

3. A summary table for receptor studies is needed.

4. Comments about 14C ADME studies described before apply here too.

5. Need to insert comprehensive metabolic pathway similar to that in BDE-99 document.

6. In most of the in vitro and in vivo animal studies that are presented in these documents, oily vehicles were used (corn oil etc.). I found this problematic. That is because large number of bromine atoms on a phenyl ring imparts several electrophillic and lipophilic properties to the aromatic ring. The increased lipophilicity will significantly alters the distribution and tissue uptake of BDE between the oily vehicle and the biological system with its hydrophilic / lipophilic properties. These conditions lead to decreased absorption and distribution with subsequent alteration in metabolism and excretion with little correlation to real occupational and environmental conditions.

7. Rational for driving RDF and Conclusions are appropriate and transparently presented. A summary table for all available studies that could be used for the estimation of RFDs should be included. This table will clarify why a particular study was the most appropriate for the estimation of RFD.

BDE-209

1. The cancer risk derived for BDE-209 is based on very high doses utilized in a two and half decade old study. These doses could not be occupationally or environmentally possible except in accidental conditions.

2. Like other toxicological reviews of other BDEs, ADME evaluations in animals are un-objectively presented. There are several summaries of several studies but no connection and limited interpretations of the data. The proposed metabolic pathway presented in for BDE-99 is very helpful. Similar pathway should be presented for this and other congeners.

3. Due to the conversion of higher molecular weight BDEs (those with larger numbers of bromine atoms) metabolic relationship between higher and lower congeners of BDE exists. Therefore, a comprehensive metabolic profile of all these compound should be presented in every toxicological review for each individual BDE.

4. Comments on the radioactive compound, its purity and specific activity that are described before, apply for this and every other congener.

5. Extensive number of receptor studies is presented in the document. A comparative summary with references will be helpful for the reader to easily conclude which is the most sensitive receptor for this congener (and other ones).

6. Concerns regarding Uncertainty Factors described before, apply here for BDE-209, too.

Richard Bull, Ph.D.

Editorial comments:

1. The Agency should reconsider the traditional organization of these review documents. The old organization is becoming very cumbersome as more and more data become available that bear on the issue of mode of action or corroborating data that support the documents overall conclusions. In this particular set of documents, the artificial separation of the neurobehavioral studies and neurochemical data over three categories (reproductive/developmental studies, neurotoxicity and Other studies) really made these difficult documents to review. I suggest that all of the data that contribute to a cohesive understanding of a particular toxicological effect need to be included in the same section. To pick a specific case, all data relevant to the neurodevelopmental effects of BDE-99 should be presented together, whether the data relate to neurobehavioral, neurochemical, or gene expression data in the CNS.

Related to this point, it is also suggested that conclusions that are derived from explorations of alternative modes of action for a particular effect be expressed more categorically. For example, there have been some investigation of contribution of thyroid hormones changes to the neurodevelopmental effects of the BPDEs. The only clear results with respect to the thyroid hormones is that of Zhou et al (2002), where effects of a different mixture (DE-71, a mixture of tetra and penta PBDEs) on thyroid hormone levels were described. The doses required to produce such effects were not far off those that produced neurodevelopmental effects with BDE-47, but were much higher that the doses of PDE-99 that produced neurodevelopmental effects. Thyroid hormone levels were examined in a study of adults treated with BDE-47 by Hallgren and Darnerud (2002), but only FT4 was reduced, not thyroxine, and the dose required to produce this effect was much too high. Other studies with the PBDEs appear to be negative, but in some cases the actual doses utilized were not provided in the document (e.g. the Hakk et al. 2002 study cited in the BDE-99 document). To this reviewer there is no basis for suggesting that the neurodevelopmental effects observed with the PBDEs are related to thyroid hormone-related effects. This actually raises concerns, rather than lowering them. If a thyroid hormone-based mode of action were identified, there would be less of concern because the risks associated with this mode of action are reasonably well understood. Therefore, a clear conclusion should be drawn that says it appears unlikely that modified thyroid function plays a role in the neurodevelopmental effects observed with this class of compounds. Similar statements should address other modes of action that have been found to be consistent with or inconsistent with respect to particular toxicological effects. In the absence of a particular toxicological effect, these data are of little use. It is really important to begin to make these distinctions as the "presumed mode of action data" may frequently form the bulk of the available data on a compound and this information needs to be placed into better context.

2. The data on PBDE occurrence in biological samples involve relatively small populations and may not be representative of either the U.S. or the World populations. Nevertheless, there are observations that imply an evolution of exposures that are somewhat different in the U.S. and other parts of the world. Similarly, there appears to be a pattern of exposures, reflected in tissue measurements, that is increasing in recent years (presumably because of the recent introduction of these compounds in new industries). These are important issues and need to be presented more proactively – i.e. in a way that supports or denies these apparent trends in exposure and providing a specific a basis for these observations, if true. As the section now stands, it simply iterates studies in a more or less sequential way, providing some casual notion of the existence of these

patterns, but not really determining whether the databases are strong and representative enough to support these conjectures or not. A few specific comments, drawn largely from the BDE-47 document as much of this information is repeated in the subsequent documents, which illustrate the problematic nature of some the discussions that were provided in the document are provided below:

a. There are several places in the discussion of data obtained with 14C that need to be clarified. Either the document poorly explains the nature of the data that is summarized or it has been misinterpreted. One example of a problem in interpretations of greater concentrations of 14C in tissues following a series of doses of non-radiolabeled compound. Such observations are frequently the result of isotope effects (e.g. the prior exposure results in a tissue pool of compound in tissues that is significantly larger than in control animals. As a result more isotope remains in the tissue pools as it becomes diluted in specific activity). The document suggests that these data reflect is a magnification of amounts of chemical that is retained with subsequent doses. This is unlikely. The only way this can be dealt with quantitatively is if the specific activity of the chemical is determined in each tissue for the single dose without prior treatment vs. that observed with a dose after prior treatment with non-labeled chemical.

b. The frequent suggestion that a smaller fraction of dose was absorbed with increasing dose as evidence of saturable absorption may also be inappropriate. There are other possibilities that have to be entertained. In the case of compounds with chemicals of such limited water solubility, such observations may well be explained by limited access to membranes because of low solubility and, more important, the limited solubility in body fluids to carry away the compound from its site of application. The solubilities of these compounds in water are listed as BDE-47 = 11 µg/L, BDE-99 =2.4 µg/L, BDE-209 = <0.1 µg/L, BDE = 0.9 µg/L. The Hughes et al. 2001 study of passage of BDE-209 through mouse skin in vitro would be plagued by this problem unless a perfusion system was used (not stated in the document). Incidentally, the doses applied in this preparation were given in amounts, not concentrations. It is essential to know concentrations to interpret these in vitro studies. The limited solubility could even affect the data obtained with 14C-labeled compounds (e.g. Viberg et al.) because these generally much smaller doses (e.g. 2.2 mg/kg) still exceed the solubility in water by a 4 orders of magnitude in the case of BDE-209. The authors of the papers reviewed may have addressed these issues, but it did not come through in the Toxicological Reviews.

The in vivo studies that employed huge concentrations in the diet would certainly have the same problem. In fact, one wonders whether the lack of clear dose-response in the NTP study of BDE-209 might reflect this problem. Equivalent responses may have been observed at much lower doses. In my view this is a real concern for estimating cancer risk from these data.

3. It is nice to have a reasonably complete discussion of the metabolism of the PDBEs in the IRIS documents. Nevertheless, there is a need to address some confusing aspects of the discussions of uptake, metabolism, distribution, and elimination of compounds in these documents rather than simply reiterating the results. One way of reducing the confusion might be a summary at the beginning of this section that lays out what appears to be happening, even to providing the conclusions of the section up front. This would avoid being surprised by the apparent finding that urinary elimination in mice, for example, appears dependent upon binding of the parent compound to a urinary protein at the end. As the descriptions are laid out, the reader is continuously struck by what appears to be results that appear contrary to general rules (e.g. that non-polar compounds are not efficiently eliminated in the urine).

There are differences among studies related to the apparent extent of metabolism of the compounds and the extent to which metabolites occur in the excreta that are presented without comment. If at all possible, this issue should be driven to conclusions that are useful in making judgments related to how harmful these compounds are. If the information is not useful or conclusions cannot be drawn, this should be stated and the presentation of this material substantially shortened.

Part of the confusion arises from the apparent reliance on measurement of 14C in these studies. These measurements are intermixed with some direct chemical measures, but that is frequently not made clear in the Toxicological Reviews. While these sections read well and are unlikely to be questioned by a casual reader, the informed reader immediately gets distracted by the methodological questions and feels that the apparent conclusions require challenge. Furthermore, questions of metabolism, covalent binding, and distribution are not possible simply by measuring the 14C.

Some specific points in the text of the BDE-47 document are referred to below where the interpretation of ADME data is ambiguous are provided below:

p. 14, 3rd para. This is an example where the legitimacy of the interpretation that there are different amounts absorbed from a dose of radio-labeled compound was administered on day 1 vs. after 10 days of administration of non-labeled compound needs to be questioned.

p. 17, second para in after Metabolism title. The last two sentences appear contradictory.

p. 17, last para. How is "covalently bound" defined (or measured)?

P. 18, 2nd full para. These results for the last day are likely to reflect accumulated metabolites from the prior exposures. Therefore, it is inappropriate to compare the amount of metabolite observed after day 1 to day 10.

p.22, 2nd par. Fifth line. It is not clear where the half-life is being measured. Was it actually in the perirenal fat or was it in the blood? The writing implies that it is in the perirenal fat but the wording is not definitive. This needs to be very clearly stated as most half-life measures are made in blood and that half-life is used to predict turnover in tissues that are sinks (e.g. fat)

Lucio Costa, Ph.D.
Additional comments

BDE-47

p. 9 Discussion on levels in human milk could be expanded.

p. 17 It is unclear why uptake of BDE-47 in cultured neuronal cells in the presence of 10% horse serum "is likely to be more representative of in vivo conditions".

p. 39 It is unclear why data on exposure to BDE-47 in relationship to thyroid hormone levels cannot be used for deriving RfD. The study of Hallgren and Darnerud provides a NOAEL of 6 mg/kg/day and a LOAEL of 18 mg/kg/day. Changes in mixed function oxidase system that were observed at 6 mg/kg/day may be discounted, as suggested.

p. 40 The important issue of pup vs. litter as the statistical unit is discussed, with the indication that the use of more than one pup/litter in the Eriksson et al., 2002 study may bias the results. Yet, in the footnote, a study by Eriksson et al., 2005 (only in abstract form) with BDE-99 is discussed, in which this same issue was shown not to influence the outcome. Perhaps this should be integrated in the main text.

p. 41 An UF of 3 for single vs. chronic exposure may not be necessary. The concept of "windows of susceptibility" during brain development would argue that chronic exposure may not necessarily result in greater adverse effects, but rather that even a single exposure at a specific sensitive time-point may elicit the highest effect. Eriksson et al. have shown with other compounds (e.g. BDE-99) that a single exposure on PND10 is the most sensitive time point. This comment would apply to other BDEs as well.

BDE-99

p. 29	Data on nicotinic receptor changes from the Viberg et al. 2004b study could be presented here. Refer here to data on p. 49.
p. 46	Here and elsewhere, when referring to Casarett and Doull's Toxicology textbook, the most recent edition (2001) could be used.
p. 48	Better references than Klaassen, 1996 or Ankenberg, 2003 could be used to discuss distribution and functions of cholinergic receptors.
p. 48	Discussion of the Ankenberg, 2003 study could be shortened, as it is not of much relevance. It is also presented unclearly.
p. 49	Choose reference other than Klaassen 1996, to indicate effects of atropine. Also, specify % decrease of 3H-QNB binding.
p. 51	Section 4.4.3 (neurotoxicity) should be renamed, as several previous sections (e.g 4.3.1, 4.3.2) already deal with developmental neurotoxicity. Eriksson is also a co-author of the proteomics paper by Alm et al. discussed here.
p. 53	Additional in vitro mechanistic experiments (see references above) may be added here and in section 4.5.3 on mode of action.
p. 56	Data on oxidative stress and BDEs (see references above) may be added here.
p. 57	In section 4.7.2 the reference Branchi et al. 2002 may be added to indicate lack of gender-specific effects.
p. 65	Use of an UF of 3 for extrapolation from subchronic to chronic may not be necessary (see comment for BDE-47). Also, given the availability of several developmental neurotoxicity data on BDE-99, an UF of 10 for database uncertainty seems excessive.
p. 68	The overall confidence in the RfD determined for BDE-99 is listed as low, same as in case of BDE-47. However, given the existence of multiple studies corroborating the main conclusions, confidence level may be raised to moderate.

BDE-153

p. 18	The % decrease of nicotinic receptors in the study by Viberg et al. 2003a could be indicated (see p. 23).
p. 28	UF of 3 for subchronic to chronic may not be necessary (see comments for BDE-47).

BDE-209

p. 12 The possible debromination of BDE-209 to lower bromine congeners may be better discussed, if possible. Should also environmental debromination be mentioned?

p. 16 Half-life may not be necessarily directly linked to rapid metabolism.

p. 38 Content of section 4.5.1 is not in tune with title of section.

p. 58 An UF (e.g. 3) for deficient available database may be added. While, differently from other BDEs, studies are available on subchronic, chronic and developmental toxicity (all yielding NOAELs or BMDs substantially higher than that from the stuies of Viberg et al), no other developmental neurotoxicity evidence is available.

Report is at times repetitive, and could be shortened. For example, results of the Viberg et al. 2003a study are described on p. 10, 33-34, 41-42, 50 and 53.

Ralph Kodell, Ph.D.

Miscellaneous comments

General

The presentation of the data and the derivation of RfDs might benefit from a unified presentation in a single document, instead of four separate documents. In particular, similarities and differences in ADME could be addressed in a cohesive manner.

Specific

BDE-47

Section 3.1, last sentence: It seems that the relative absorption rates of rats and mice are not ~~qualitatively the same in the two studies compared, contrary to what is stated.~~

Page A-2: The AIC is highest for the selected linear model, which fits best in terms of the p-value. For BDE-209, page A-10, low AIC seems to be one of the selection criteria, along with high p-value. I believe the selection criteria should be consistent. AIC is sometimes used as a weight for averaging the results of several models. It might be a better criterion than p-value.

Page A-2: The indication is that modeling was done for both males and females. But, there were no female data.

BDE-99

Page 81: The Hill model fits best in terms of its having the highest p-value. However, it also has the highest AIC. This isn't consistent with BDE-209, where low AIC is one of the criteria for model selection. AIC should be used consistently.

BDE-209

Page 21: How can 99 mg/kg-day be characterized as a NOAEL in the study by Carlson (1980) when it was associated with a statistically significant increase in the liver-to-body-weight ratio? (Same in Table 2, page 19)

Page 32, lines 5-8: I strongly disagree with the conclusion by Eriksson et al. (2005) regarding litter-based studies. This sentence should be re-stated so that it doesn't sound like this conclusion is accepted as fact by EPA. In general, this conclusion is erroneous.

Page 34, lines 13-15: There is something wrong with the sentence. A decrease in disruption of habituation is not an adverse effect.

Page 38, lines 6-3 from bottom: There is something wrong with this sentence. Thyroid tumors were seen in females as well as males, but they were not significant in either sex. Why is NTP (1984) cited?

Page 39, lines 12-11 from bottom: There is the same problem regarding the statement about thyroid tumo

External Peer Review

Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs) Human Health Assessment

FINAL REPORT

Prepared for
Integrated Risk Information System (IRIS) Program
Office of Research and Development
National Center for Environmental Assessment
U.S. Environmental Protection Agency

Prepared by
ORISE IRIS Technical Assistance Team
Oak Ridge Institute for Science and Education
Oak Ridge Associated Universities

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Toxicological Review for Polybrominated Diphenyl Ethers (PBDEs)

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Notice: EPA modified this report in August, 2007 to include only four of the five reviewers' comments. One reviewer's comments were excluded from the report and were not considered by EPA due to the perception of a potential conflict of interest.

EXTERNAL PEER REVIEWERS

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The ORISE IRIS Technical Assistance Team has neither altered nor edited these comments for grammatical or other errors.

Peer Review Project

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The U.S. EPA's National Center for Environmental Assessment (NCEA) has developed several draft Toxicological Reviews for Polybrominated diphenyl ethers. Specifically, toxicological review documents have been developed for tetra-, penta-, hexa-, and decabrominated diphenyl ethers. The charge questions below specifically address the polybrominated diphenyl ethers assessment.

GENERAL QUESTION

Are you aware of other published peer-reviewed toxicological studies not included in these Toxicological Reviews that could be of relevance to the health assessment of BDE-47, BDE-99, BDE-153 or BDE-209?

Ahmed Ahmed, Ph.D.

I have examined the available literature, for the past 10 years, for BDE-47, BDE-99, BDE-153, and BDE-209 by searching under their individual chemical name and chemical abstracts number (CASRN) and crossing the outcome with adverse effects, cancer and/or systemic or genetic toxicity,. I found about 200 citations and their abstracts which represent various types of studies on these compounds. The majority, if not all, of these references are included in various "Toxicological Review" document for one or the other of these chemicals. A detailed literature search analysis is included in this report. The authors of the document may need to verify the existence and use of the appropriate citations in the reviews using the reference manager software programs.

The Toxicological reviews for BDE-47, BDE-99, BDE-153, and BDE-209 are extremely detailed and commonly repetitive. The same information is repeated several times in the same document under different headings (subsection) and in documents for other congeners. Although these repetitions are distracting, I realize they are pluses rather than negatives, I believe that was done to emphasize particular point or effect, to establish the validity of a study and its results and to point out the drawbacks in experimental design or data analysis and interpretation. Therefore, I find the quality of these review documents in a "good to excellent" range. In some of these reviews however, the lack of scientific information makes the decision making processes difficult due to limited number of studies or narrow scientific objectives that disregarded other possible interpretations. This problem does not point to any shortcomings in the efforts of the authors of these documents. Rather it indicates the limitation and shortage of available information (studies).

In a general sense, these chemicals are congeners of each other and because each one is contaminated by one or more of the others. Also, they metabolically, under environmental and biological conditions, are inter-convertible to each other (compounds with higher bromine numbers are converted to compounds with lower bromine). Therefore, I believe that putting them all in one comprehensive review document would serve the purpose more adequately. They almost have the same toxic end points with varying degrees. The effects of these compounds, which came from limited number of studies, are repeatedly compared in each document for each individual compound.

Metabolic and distribution studies are extensively described in the document without deep scientific interpretation of the results nor how these results could be interpreted in the evaluation of human body burden. Furthermore, the purities of the radioactive chemicals used in most studies were not cited. The position of the label as well as the specific activities of the 14C compounds, used in these studies were not indicated in most sections. I am also troubled by the different ways used for the presentation of the doses and concentrations of the compounds and their metabolites in biological tissues (umole, ug, percent of the dose). A unified parameter should be used to insure comparative analysis and easy follow up.

Richard Bull, Ph.D.

I am not aware of other peer-reviewed toxicological studies that would contribute to an understanding of risks associated with these PBDE's. However, some papers included in the review should be better integrated into the derivation of the reference doses.

Lucio Costa, Ph.D.

There are a number of publications that have not been included in the Reviews and that may be relevant to the health assessment of BDEs.
A few studies indicated that house dust is a major source of exposure to BDEs, and for toddlers in particular, dust has been estimated to account for 80% of BDE exposure.

- Jones-Ortazo HA et al., Environ. Sci. Technol. 39: 5121-5130, 2005
- Wilford BH et al., Environ. Sci. Technol. 39: 7027-7035, 2005
- Schecter A et al., J. Toxicol. Environ. Health Part A 68: 501-513, 2005

Contamination of food with BDEs has not been mentioned, yet diet is believed to contribute to the overall body burden of BDEs.

- Hites RA et al., Environ. Sci. Technol. 38: 4945-4949, 2004
- Schecter A et al., Environ. Health Perspect. 114: 1515-1520, 2006

High levels of BDEs were found in children (case study).

- Fischer D et al., Environ. Health Perspect. 114: 1581-1584, 2006

Levels of BDEs were recently determined in plasma of pregnant women in California.

- Bradman A et al., Environ. Health Perspect. 115: 71-74, 2007

Various studies have explored possible mechanisms of action of BDEs, including activation of protein kinase C and induction of oxidative stress.

- Kodavanti PRS, Derr-Yellin EC, Toxicol. Sci. 68: 451-457, 2002
- Kodavanti PRS et al., Toxicol. Sci. 88: 181-192, 2005
- Reistad T, Mariussen E, Toxicol. Sci. 87: 57-65, 2005
- Reistad T et al., Arch. Toxicol. 80 : 785-796, 2006

Ralph Kodell, Ph.D.

I am not aware of any other relevant studies.

1. QUESTIONS RELATED TO THE DERIVATION OF THE REFERENCE DOSE

FOR BDE-47, BDE-99, BDE-153 and BDE-209

1.1 Have the rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies been transparently and objectively described in the draft

Toxicological Reviews of BDE-47, BDE-99, BDE-153 and BDE-209? Are there additional studies that should be considered for deriving the RfDs for any of the four PBDE congeners?

Ahmed Ahmed, Ph.D.

In all the documents provided, except for BDE-209, no cancer related data was available. In each individual document for every compound there were several sporadic, non cancer related, referenced molecular and systemic toxicological studies. Most of the available and presented studies, unfortunately, toxicological and molecular (receptor binding etc.), were designed to look for the effect(s) of these modern environmental pollutants in light of the toxicological effects of traditional and well studied compounds such as PCB. The large numbers of the reported molecular studies on BDEs were tailored after the effect of poly chlorinated aromatic hydrocarbons. Although the chemicals under review (BDE) are halogenated (brominated) aromatic hydrocarbons, these tailored studies back fired. That is because we ended up with a number of negative or nonspecific effects and obtained limited information to use for the proper evaluation of the risk from BDEs.

The few available systemic toxicological studies are blemished by the fact that most of these studies came from the same laboratory. Although, the data seems to be academically solid, their validity and strength is debatable because it has not been verified in various other laboratories neither in the U.S. nor in other countries. This factor alone weakens but not hinders the derivation of the specific RFD. It makes the confidence in these RFD's low

The authors of the Toxicological Reviews for BDE-47, BDE-99, BDE-153, and BDE-209 have to base their derivation of RFD on continuous scientific information. They used those studies that have specific doses and defined time of exposure as well as a defined adverse effect(s). The only available studies that have dose response and time course were those described by the authors in ~~the texts and were used for the derivation of RFDs. With this in mind, they have clearly and very~~ transparently derived the rational for using these studies. They also took into consideration all drawbacks that weakness each particular study. I was impressed by the way they listed at least 6-10 points explaining their concerns for the use of particular data, in each selected study, in the derivation of RFD for each individual compound. Meanwhile they documented the rational for using the study in their derivation of RFD. There was very clear presentation of the pros and cons of each study utilized in the estimation of RFD.

Richard Bull, Ph.D.

The data available on most of these compounds is quite limited (BDE-209 being somewhat of an exception). In most cases, the risk assessment focuses solely on results from a non-conventional neurodevelopmental test. In one case, BDE-209, a conventional reproductive/developmental toxicity test found no effects at doses much higher than observed in the neurobehavioral study. This may reflect the insensitivity of conventional reproductive/developmental toxicity tests OR more likely, increasingly smaller fractions of the doses being absorbed as doses are increased. The doses utilized were huge, 100, 300 and 1000 mg/kg in corn oil. One would predict that the aqueous phase through which these compounds would have to diffuse to get to an absorptive surface to be exceeded at doses orders of magnitude lower than the lowest dose! Nevertheless, the discrepancies raise significant issues with the standard application of uncertainty factors to results that are clearly more sensitive than conventional methodologies. To put this starkly, either the UFs applied to the "standard" test data are way too small OR smaller UFs need to be applied to these data must be adjusted to account for their much greater sensitivity (and specificity).

There are particular UFs that appear completely inappropriate in the current derivation of reference doses. For example, defaulting to a database uncertainty factor when data of this relative sensitivity to conventional evaluations of reproductive/developmental results are available is very inappropriate.

A more central role also needs to be given to the neurochemical data that is provided, especially those that utilized essentially parallel study designs to the neurobehavioral studies. They are presented as supporting data. They are a lot more than that. They provide an organic measure of modified neural development. It may not be entirely clear how the neurobehavioral and neurochemical data are linked functionally, nevertheless, the two data types contribute as an independent measures that there is an apparently permanent alteration in development. This type of corroborating data should be taken as being much more critical than data from 'standard protocols'. Targeted data of this kind in developmental neurotoxicity would be useful if broadly available. It is simply too expensive and time consuming to identify "critical" endpoints for every compound subjected to safety assessments when the expectation is that such effects are relatively rare. The neurobehavioral data may still be the most appropriate to use for the dose-response assessment, but in a sense the neurochemical data are the critical information. Until I found that data in the documents, I was teetering to the point of saying neurobehavioral data was an inappropriate, unsupported, and poorly understood endpoint (despite what is said in the guidelines).

The more critical question with the apparent developmental impacts of the PBDEs is the apparent consistent developmental neurotoxicity that is seen within this class of compounds. This is observed despite very different patterns of metabolism, distribution, and persistence of these compounds in the body. Some effort should have been expended to see if the relative potency of the PBDEs could be rationalized considering the differences in the extent of metabolism.

On the other hand, one has to be concerned that very similar data have been generated by this same laboratory on a broader set of unrelated compounds. It is time to be concerned about the specificity of these data for developmental neurotoxicity. Independent confirmation is essential when such a apparently non-specific endpoint ends up flagging everything studied.

I most strenuously object to the treatment of these single-dose experiments as being equivalent to a subchronic exposure when applying uncertainty factors to arrive at an RfD. This is justified on the basis that brain development does not occur at an equivalent rate over a lifetime. This question is very relevant to whether of not a body burden approach should have been taken for this endpoint. Scientifically, the question is whether a body burden accumulated over time before the critical period would have the same impact as tissue levels that were achieved by the single dose protocol that was used. The available data do not allow this possibility to be evaluated. Therefore, the assumption that the acute dose at PND 10 is equivalent to a subchronic exposure is highly suspect.

Obviously, the data that are available are not sufficiently developed to allow the development of PK models. However, if evaluated critically (i.e. all the data are not equally informative as indicated in the editorial comments appended to the response to the formal questions) there may be enough absorption, distribution, and elimination data to make some ballpark estimates of consistent measures of how much of the parent compound and/or metabolites are present in tissues. The essential question is whether the effects of 1/10 the dose administered between PND 0 and PND 10 are the same as the full dose that is administered that is administered on PND 10. This experiment or an analogous one has not been done. Therefore, no conclusions can be made. Until such data are available, these studies have to be treated as a single dose studies, not a subchronic exposure.

There is some serious question related to whether the anti-thyroid effects of these compounds are of importance to the neurodevelopmental effects observed. The data of Zhou et al. (2002) establishes that the antithyroid effects are observed with DE-71, a formulation that might be reasonably linked to neurodevelopmental effects observed with BDE-47 and BDE-99. The Zhou et al. (2002) study was very well done and included not only good dose-response information, but a probable mechanism for the observed effects on thyroid hormone(induced metabolism of thyroid hormone metabolism). As pointed out in more detail in the editorial comments below, the thyroid effects seen in this study occur at doses that are higher than those that produce the neurodevelopmental effects of BDE-47 and BDE-99. As a result, the conclusion needs to be made that the neurodevelopmental effects cannot be linked to the anti-thyroid effects of these compounds.

Lucio Costa, Ph.D.

The rationale and justification for deriving RfDs on the basis of neurobehavioral toxicity studies have been well described and documented. The additional studies indicated above, particularly on body burden in infants and toddlers, would strengthen the health assessments, though they will not change the final determination of RfDs.

Ralph Kodell, Ph.D.

Limited human data do not indicate an association between exposure to PBDEs and adverse health outcomes. However, these data are insufficient to conclude that there is no potential for such effects. For BDE-47, BDE-99 and BDE-153, neurobehavioral effects are the only toxic effects that have been observed consistently in rodent studies of PBDEs, and therefore provide the only data for deriving RfDs. For BDE-209, the NTP rat and mouse bioassays (NTP, 1986) provide suitable data on noncancer endpoints other than neurobehavioral endpoints. The rationale for basing the RfD for BDE-209 on neurobehavioral effects instead of the other effects is that the neurobehavioral effects lead to the lowest point of departure. The rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies is transparent and appears to be objective. I do not know of additional studies that should be considered for any of the PBDEs. However, among the studies that have been considered, I think that greater consideration should be given to some of the studies other than the Eriksson/Viberg studies. Specifically, the studies of Branchi et al. (2002) and Kuriyama et al. (2005) provide data on BDE-99 that is suitable for deriving an RfD. The Branchi data have not been modeled while the Kuriyama data have been modeled but not used.

As noted in the documents, an association between neonatal exposures to BDE-47, BDE-99, BDE-153 or BDE-209 and neurobehavioral dysfunction in humans has not been established. Nevertheless, the behavioral studies appear to provide the most appropriate, dose-response data on adverse noncarcinogenic effects on which to base the health assessment of the four PBDE congeners.

1.2 Do you agree or disagree with EPA basing the health assessment of BDE-47, BDE-99, BDE-153 and BDE-209 to a large extent on the Eriksson/Viberg neurobehavioral studies?

Ahmed Ahmed, Ph.D.

As described earlier, the limitation of the availability of complete and comprehensive one or more studies that evaluate various types of adverse effects of these chemicals necessitated the utilization of what is available such as Eriksson & Virberg neurobehavioral studies. It is well known that there could be no one complete and comprehensive toxicological study. Every individual study will have its own limitation. In spite of some technical weaknesses in these studies, there use in the risk and RFD estimation is warranted.

The reason for the limitation of traditional toxicological evaluation on these newly detected environmental pollutants is because there are no extramural funds in NIH or EPA for this type of studies in the United States of America. That is why we ended up using studies from overseas to set up risk evaluations in the USA. This seems disturbing, specifically if we realize that the concentrations of these chemicals are estimated to be about 10-15 times higher in the biological fluids and tissues of American citizens as compared to European (specifically Swedish) citizens. I urge the responsible agents to encourage the classical toxicological evaluation of these compounds not in light of being similar in their structure to other compounds but in light of the fact that they are highly lipid soluble compounds that form depot in particular tissues of the ecological and mammalian biological systems. These depots create guaranteed life long exposure to these Xenobiotics, even after these chemicals are removed from the environment. The placental storage and transfer (if any) of these chemicals will turn them and their metabolites into trans-generational pollutants.

Richard Bull, Ph.D.

I do support the use of the neurodevelopmental studies for the purpose of deriving points of departure. As intimated above, however, considered alone, these endpoints have too little specificity to be of great concern. There are four fundamental issues: 1) The central importance of parallel neurochemical findings has not been used to advantage (or at least to the advantage it could be), 2) the interpretation of the neurobehavioral data as decreased habituation should be more critically evaluated, 3) the assessments of all the BPDEs depend upon results obtained from a single laboratory, and 4) the overwhelming application of uncertainty factors to such a subtle effect (i.e. relative to the usually accepted protocol) needs to be reconsidered. The first issue was addressed in question 1. The other three are discussed below:

It would have been better to present the actual behavioral data in the document rather than the habituation ratio. This ratio clearly is affected by both the depressed activity seen in the first period and the higher activity seen in the third period. The use of the habituation ratio forces an interpretation that may not be appropriate (or at least the reasons for selecting this parameter was not justified sufficiently in the documents or in the original papers). From the qualitative description of these data that was provided in these documents, they could be interpreted, with equal, if not greater, validity, as a depressed reaction to a novel environment and/or sustained hyperactivity.

Scientific findings need independent confirmation. Thus, EPA should be concerned about placing so much emphasis on set of studies that are generated completely within one laboratory, especially when the methodology and design are peculiar to that laboratory. Although it is not identified in the document, there is corroboration of the findings of Viberg and Eriksson with one compound (PBDE-99) in the study of Kuriyama et al. (2005). The experimental design was somewhat different. Nevertheless, the authors observed an increase in activity at PND 36 with a single dose of 300 µg/kg to the dam on GD 6. The measurement of activity after the animals had habituated to the test system, so the data are comparable to the activity observed in the 40-60 minute interval in the Eriksson et al. (2002) paper. Moreover, the lowest effective dose was somewhat lower than that reported by Eriksson and there is a clear NOAEL at 60 µg/kg.

It must be noted, however, that the implied relationship of the effects of PBDE-99 to altered thyroid function is not substantiated in Kuriyama et al. (2005). The doses producing the neurobehavioral changes occur at too low of a dose to be attributed to changes in thyroid hormone. In general, all the documents need to be more rigorous in their treatment of so-called "mode of action" data.

The application of group of uncertainty factors to a NOAEL despite the fact that the basis of this effect is not established and the apparent subtlety of the response relative to conventional developmental studies is not appropriate. This is discussed in some detail in the answer to question 1.5.

Lucio Costa, Ph.D.

Given the limited body of toxicological information available, use of the Eriksson/Viberg neurobehavioral studies as a basis for the health assessment is the proper approach.

Ralph Kodell, Ph.D.

The study of Eriksson et al. (2001) is the only available toxicity study with dose-response data on adverse (neurobehavioral) effects from exposure to BDE-47. The study of Viberg et al. (2004) has dose-response data on BDE-99. However, the studies of Branchi et al. (2002) and Kuriyama et al. (2005) also provide dose-response data. The data from Kuriyama were modeled and compared to the results from modeling the Viberg data, but the results from the Viberg study were selected for deriving the RfD. The reason for not using Branchi et al. (2002) for modeling is that there is an inversion at the highest dose. This does not seem to be a compelling reason to avoid modeling the data at the other doses. The study of Viberg et al. (2003a) is the only study with dose-response data on adverse effects for BDE-153. For BDE-209, the NTP rat and mouse ~~bioassays (NTP, 1986) provide suitable data on noncancer endpoints as does the neurobehavioral~~ study of Viberg et al. (2003b). Data from these studies have been evaluated and compared. There seems to be no alternative to basing the health assessment of the four PBDEs to a large extent on the Eriksson/Viberg studies, but the additional modeling for BDE-99 should be done and compared to Viberg (2004).

1.3 Are the Eriksson et al., 2001 (BDE-47), Viberg et al., 2004 (BDE-99), Viberg et al.,2003a (BDE-153) and the Viberg et al., 2003b (BDE-209) studies appropriate for determining the point of departure? Have the strengths and weaknesses of the Viberg and Eriksson studies been appropriately characterized and considered?

Ahmed Ahmed, Ph.D.

Following my review of the original reports, I found that Eriksson et al, 2001 (BDE 47), Virberg et al, 2004 (BDE-99), Virberg et al., 2003 (BDE-153) and Virberg et al, 2003b, 2003 (BDE-209) represent the most relatively complete studies on dose/response (neurobehavioral effects) relationships in animals. Most other available studies, discussed in these documents, could not directly correlate or tie the dose response and time course relationships. My main concern is that all these studies are coming from one group of scientists who pioneered the neurobehavioral / ADME (distribution in rodents) evaluation of these chemicals. With this information, come the problems of lack of validation of data coming from one laboratory with other data coming form other laboratories on the same scientific issues. Nevertheless, the authors of these reviews have clearly and transparently judged these studies without biased. They expressed the weakness of each study as well as its strengths in their utilization for driving the RFDs. The authors should be commended on their unbiased evaluation.

Richard Bull, Ph.D.

It is my opinion that these data are appropriate as long as it is emphasized that the neurochemical data that have been collected using parallel protocols add significant support to the conclusion that a modification(s) of the normal developmental pattern occurs as a result of these treatments. Please note that other neurobehavioral data were identified in the PBDE-99 document that should have been more formally considered as indicated in the response to question 1.2. Moreover, the data sets on activity per se are much more appropriate for dose-response assessment than the habituation ratio, for reasons provided above. The habituation ratio is derived data, but the data provide very little support for the idea that loss of habituation is the basis of these results.

Lucio Costa, Ph.D.

The studies by Eriksson and Viberg are unusual, as indicated in the reports, but are the only available for most BDEs. At this stage, they are the only ones available for determination of point of departure. However, the study of Kuriyama et al. (2005) should be considered for determination of point of departure for BDE-99. Strengths and weakness of these studies have been described appropriately (but see comments below). A sentence may be added to indicate that further developmental neurotoxicity studies are needed for BDEs.

Ralph Kodell, Ph.D.

The Eriksson et al. (2001) study appears to be the only study available with data that might be used to determine the point of departure for BDE-47. For BDE-99, data from several candidate studies are modeled for determining a point of departure. The Viberg et al. (2004) study appears to have the best dose-response data and to provide the best model fits. However, the data from Kuriyama et al. (2005) also fits acceptably and gives lower BMDLs for some endpoints. Reasons were given for choosing the Viberg-derived BMD over the Kuriyama-derived BMD, but I think the Kuriyama-derived value is equally justifiable. The only well-designed dose-response study with dosing both pre-natally and post-natally (Branchi et al., 2002) was not modeled because of an inversion at the highest dose. Conceivably, these data could be modeled for BMD estimation, perhaps by omitting the highest dose, as is sometimes done with cancer incidence data. The Viberg et al. (2003a) study is the only study with dose-response data for determining a point of departure for BDE-153. Both the NTP bioassay in rats and mice (NTP, 1986) and the study of Viberg et al. (2003b) in mice provide data appropriate for determining a point of departure for BDE-209. Of these, the Viberg et al. (2003b) study gives the lowest point of departure, and is thus selected.

A clear weakness of the Eriksson/Viberg studies is that they did not conform to health effects test guidelines for a neurotoxicity screening battery or developmental toxicity studies. The dosing regimen did not include gestation and lactation exposure, and only single doses were administered. More than one pup per litter was used for behavioral testing, thus confounding dose effects with litter effects. (Although the authors reported doing a split-plot analysis of variance in all four primary papers, which would correctly recognize and use the litter as the experimental unit for testing treatment effects, their pair-wise testing for such effects appears to have treated each pup as an independent experimental unit.) In the cases of BDE-153 and BDE-

209, the dose-response data were not considered suitable for statistical modeling because only graphical information was available. These weaknesses have been characterized and considered, and offsetting strengths have been discussed. However, it is surprising that the data on BDE-153 and BDE-209 cannot be recovered from the authors to allow dose-response modeling and BMD estimation. One important weakness that was not emphasized for BDE-47, BDE-153 and BDE-209 is that the Eriksson/Viberg mouse studies were done in males only.

1.4 Have the most appropriate critical effect and point of departure been selected? And has the rationale for the point of departure been transparently and objectively described?

Ahmed Ahmed, Ph.D.

With all the above consideration the authors have critically and objectively selected the most critical effect (neurobehavioral) and established the most appropriate point of departure (dose response) for all chemicals under review. The authors have very clearly rationalized, in great detail, in each individual review, their selection of each particular point of departures.

Richard Bull, Ph.D.

Among the data that are available, the neurobehavioral data provide the best data for identifying a point of departure. There are some lingering questions that relate to effects of BDE-99 that are reflected in histologic changes that occurred in the ovaries and vaginal epithelium at very small doses (i.e. 0.06 mg/kg day). However, these data were not described with sufficient clarity in the document to determine if they should not be used (i.e. neither incidence or severity are described in the context of dose-response).

My review of the Talness et al. (2005) study does raise some issues both about design and interpretation that may have been the basis of the Agency's apparent reluctance to use the Kuriyama et al. (2005) data on PBDE-99 (although it was not stated, if that were the case). For example, it is difficult to understand the conclusion that necrosis was observed by electron microscopy (Fig 1 & 4), but were not observable by light microscopy (see p. 194, section 3.1.2). Second, the number of animals examined for changes in the vagina was very small. Further, the authors do not make clear the basis for their repeated assertion that the doses tested resulted in levels of 6-29 times greater than reported in human breast adipose tissue. Was a human study conducted that looked at single doses that gave rise to such levels? I could find no reference to such a study.

Lucio Costa, Ph.D.

The most appropriate critical effect and point of departure have been selected and the rationale has been adequately described.

Ralph Kodell, Ph.D.

Although the seriousness of decreased habituation capability as a manifestation of an adverse effect on spontaneous motor behavior is not discussed, it is a common measure of developmental toxicity across studies. Thus, it appears to be an appropriate critical effect for deriving a point of departure. However, the individual measures of decreased habituation might be as appropriate as or more appropriate than the habituation-ratio as indicators of toxicity. For BDE-153 it is unfortunate that data on neither the habituation-ratio nor the swim-maze learning/memory test could be recovered for modeling. The dose-response for the swim-maze effect might be different from the habituation-ratio dose-response. (Unfortunately, swim maze data on BDE-99 (Eriksson et al., 2001) involved only a single high dose.) For BDE-209, too, it is unfortunate that dose-response data on the habituation ratio cannot be recovered for modeling and BMDL calculation. It's not clear why the actual data on BDE-153 and BDE-209 cannot be recovered from the studies' authors, given that the studies were published fairly recently (2003). In fact, it would be good if the dose-response data for all four PBDEs could be obtained so that litter effects could be handled properly in the BMD modeling. It would be far better if a BMDL rather than a NOAEL for habituation-ratio could be used for setting an RfD for neurobehavioral effects of BDE-153 and BDE-209.

For BDE-47 and BDE-99 and BDE-209, the rationale for selecting the point of departure in terms of the BMD and associated BMR are clearly spelled out. Selecting the BMD as the dose that corresponds to a shift of 1 standard deviation in the mean (BDE-47 and BDE-99) corresponds approximately to a 10% BMD with a critical cut-off defined by assuming 1% background risk for a normal distribution with constant variance. The use of a BMR of 10% for the BDE-209 quantal noncancer endpoints is explained. I think it ought to be stated explicitly that the BMDL rather than the BMD is used for these endpoints in order to account for experimental uncertainty (variation), which is a good practice and is related to the use of uncertainty factors. (However, the uncertainty may be understated because of treating littermates as independent experimental units.) Generally, for each endpoint, the BMD and BMDL resulting from the best-fitting model (or an average of the best-fitting models: BDE-209) and/or the model fitted to the most dose groups are selected. Then, the lowest BMDL among those is selected as the point of departure. The sequential likelihood-ratio testing approach for selecting the fitted model for neurobehavioral effects of BDE-47 and BDE-99 is very sound and is explained very clearly. However, I do not understand why, in the case of BDE-99, it must be assumed that 8 animals of each sex were tested behaviorally. Can't this be clarified by contacting the study's authors?

To the extent that data are available for dose-response modeling, I believe that the selection of critical effects and points of departure are appropriate, and that the rationale for the points of departure has been transparently and objectively described. However, I think a strong effort should be made to recover neurobehavioral toxicity data from the authors (Viberg et al., 2003a, 2003b) to allow dose-response modeling and BMD/BMDL calculations for neurobehavioral effects of BDE-153 and BDE-209, and to refine the modeling for BMD-47 and BMD-99.

1.5 Have the rationale and justification for each uncertainty factor (UF) selected in the draft 2 Toxicological Reviews of BDE-47, BDE-99, BDE-153 and BDE-209 been transparently described? If the selected UFs are not appropriate, what alternative UFs would you suggest and what are the scientific rationales for those suggested? Does the database support the determinations of the RfDs for BDE-47, BDE-99, BDE-153, and BDE-209?

Ahmed Ahmed, Ph.D.

In their calculation of each individual RFD for each PBDPE, the authors have clearly classified several uncertainty factors for each compound based on the available information in the studies utilized. I found that their selection of these uncertainty factors to be well rationalized and the objectivity of each uncertainty factor to be very clear. It was apparent that the number assignment was very uncertain during the panel meeting on Feb 22,2007. It seemed very uncertain whether several UFs should be assigned a10 or 3.

In considering acute versus chronic uncertainty factor, I feel that the accumulation of BDEs, specifically the lower brominated compounds, tetra (BDE-47 and penta (BDE-99) should be considered in the calculation of their RFDs. These compounds detected in various human tissues and biological fluids and have very long half lives in human tissues; the adipose tissues in vital organs and biological fluids; breast milk. Thus, for the highly susceptible human groups such as fetuses and infants there will be continuous internal dosing that is coming from storage depots. Accordingly, the body burden for infants will not be only dependant on exposure to external dosing from the environment. It will be dependant on a combination of external (environmental) and internal factors (the depot of biological tissues and fluids). This complexity should be considered in the estimation of RFDs. Specifically for the U.S. population. In the American population, the levels of most of these chemicals in blood, tissues and biological fluids are about 10 or more times higher than that detected in biological fluids from other (European) countries. Such facts should be considered in the calculation of RFDs here in U.S.A. Finally I believe that available limited data base should support the determination of the RFDs for BDE 47, BDE 99, BDE 153, and BDE 209.

Richard Bull, Ph.D.

The rational and justification of each UF has been transparently described. However, I believe that they have been inappropriately applied to these chemicals.

There was no consideration in the document related to the specificity and sensitivity of the neurobehavioral and neurochemical measures that have been applied vs. more standard endpoints. In particular, it is inappropriate to apply the UF relative to data base inadequacies. One might consider modifying UFA and UFH as well.

Given the nature of the available data, the rationale for using an adjustment from subchronic to chronic exposures (UFS) for these data is also not sustainable scientifically. In this case, the critical issue is whether the body burden of parent compound is important. Thus, the adjustment of 3 that is made on the UFS is not appropriate. Rather one needs to consider the extent to which the mother's pre-pregnancy accumulated body burden would influence the developmental outcome. As I see no way of even making a judgment on this issue based on the available data, I suggest that UFS be raised to 10.

There is a more general problem with the database uncertainty factor when it is applied to the development of RfDs. The traditional across species and within species uncertainty factors relate to the critical endpoint being addressed in the risk assessment. The database uncertainty factor addresses questions that go beyond this endpoint and focus on risks that might occur, but there are no relevant data. Thus, it does not reflect on the accuracy of the assessment of the endpoint being evaluated. This uncertainty factor is more appropriately applied at the point that risk management decisions are being made (e.g. at the point that MCLs are being developed). This concern should be introduced at the point where other parallel uncertainties are entertained (e.g. can remediation efforts reduce the risk or whether the MCL is within a range that can be measured).

Lucio Costa, Ph.D.

The selection of UFs has been described in detail, though I do not fully agree with some choices (see comments below for individual BDEs). The database on which RfDs are determined is in most cases very poor, particularly in case of BDE-47 and BDE-209. Perhaps RfDs should be acknowledged as "temporary", while waiting for additional studies that may increase confidence.

Ralph Kodell, Ph.D.

Default uncertainty factors of 10 for UFA and UFH are used for BDE-47, BDE-99 and BDE-153 without much explanation or justification. For BDE-209, the UFA default (but not the UFH default) has been explained satisfactorily. Taken together as a product, values of 10 each for UFA and UFH may be overprotective, but there is no alternative methodology that is currently accepted for expressing these factors as a smaller unitary factor, as might eventually be done via hierarchical modeling.

Looking at these factors separately, a UFA of 10 might at first seem conservatively large given that no evidence of an association between neonatal exposure to PBDEs and neurobehavioral effects in humans exists. On the other hand, there is no evidence to the contrary, and the mode of action is not yet understood. Because the potential adversity to humans is present, a value of 10 seems justifiable in all four cases. For UFH, I believe there is justification for deviating from the default value for all four congeners. Because the neurobehavioral effects seen in rodent studies result from exposures at critical points in early development, I believe it can be argued that the most sensitive members of the population for these effects (neonates) are already accounted for. Because the default value of 10 is used to account for differences in sensitivity among all members of a population, and because it seems hard to justify a factor that large for variation just among neonates, a smaller value of UFH appears justified. I recommend a value of 3 for UFH for all four PBDEs.

The choice of 3 for UFS for all four congeners appears justifiable to me, recognizing that timing of exposure is more critical than duration of exposure for the neurobehavioral effects observed. However, I regard this factor as accounting more for uncertainty arising from a lack of pre-natal exposure in the studies used to derive the RfDs than for uncertainty regarding potential effects of chronic exposure.

Using a value of 10 for UFD for BDE-47, BDE-99 and BDE-153 does not seem justifiable. In my opinion, if the database is so uncertain as to require a UFD value of 10, then the database is too limited to allow the derivation of meaningful RfDs. The primary neurobehavioral endpoint appears to be quite sensitive, and it is consistent across congeners. For BDE-47, I recommend a UFD value of 1. Although there is only a single study, the neurobehavioral endpoint is the same as for the other congeners, and dose-response data are available for basing the point of departure on a BMDL. For BDE-99, I also recommend a UFD value of 1. There are several studies and dose-response data are available for basing the point of departure on a BMDL. For BDE-153, I recommend a UFD value of 3. There is only a single study, and dose-response data could not be recovered for BMDL calculation. If those data can be obtained from the study's authors and used for BMDL calculation, then this factor could be reduced to 1. For BDE-209, I recommend raising the factor from 1 to 3. Granted, there are data from more than one study, and BMD modeling was done along with model averaging for non-neurobehavioral effects. However, a NOAEL for neurobehavioral effects rather than a BMDL was selected for the point of departure, because of the inability to recover the neurobehavioral dose-response data. To me, the absence of definitive data for dose-response modeling for neurobehavioral effects reflects an inadequacy in the database, and in fact, inadequacy in the very data ultimately used for deriving the RfD. If data can be obtained from the study's authors and used for BMDL calculation, then this factor could be reduced to 1.

One factor that is not mentioned is UFL for going from a LOAEL to a NOAEL, because LOAEL-to-NOAEL extrapolation is not done here. However, I think this factor should also apply when using a BMDL10 as a point of departure. A 10 % benchmark response is not negligible. A BMD10 (BMDL10) is more in line with a LOAEL than with a NOAEL. I recommend applying a UFL factor of 3 to each of the BMDL10 values to account for uncertainty in extrapolating from a dose of non-negligible toxicity to a dose of negligible toxicity.

I believe the database supports the determinations of RfDs, but I agree with the statements in the documents that the overall confidence in the RfD assessment of BDE-47, BDE-99 and BDE-153 are low. I feel the same way about BDE-209.

2. BODY BURDEN APPROACH

2.1 Are there adequate data for considering body burden as an alternative dose metric to administered doses in any of the RfD derivations?

Ahmed Ahmed, Ph.D.

The current available animal and human data regarding the body burden of BDE's are sporadically designed and extremely limited. Although there are several studies under each compound that describe the ADME or body burden concept (absorption, distribution and tissue accumulation and excretion), the kinetics (t1/2, volume of distribution, rates of absorption, metabolism and excretion) of the absorption, accumulation and removal processes of each individual compound have not been established. Similarly the identity, type and structure of the accumulated chemical species have not been recognized. In natural environmental exposure setups, there is no single (exposure) dose. Humans are continuously exposed, continuously storing, distributing, metabolizing and excreting the compounds or their metabolites. In this regard even the year or more long half life, described for some congeners, is in reality not a true kinetic factor, because the parent molecules or its metabolites are primarily stored in certain target tissues and continuously released into the blood for circulation, metabolism and excretion. These tissue stores are continuously replenished by absorbing more from the external surrounding environment. All these events should be taken when considering body burden as an alternative dose metric in the derivation of any of the RFDs. Such information is currently scarce (McDonald, 2005).

Richard Bull, Ph.D.

There may be a reason for considering body burden. As indicated in the response to questions 1.1 and 1.5, the question of whether increased body burden would contribute to the critical neurobehavioral endpoints evaluated has simply not been tested. It is for this reason that treating a single dose experiment as if it were a subchronic exposure is inappropriate. In addition, it is not clear whether the body burden or daily dose is the best dose metric for the chronic effects of those members of the PBDE class that have been evaluated in chronic studies. Therefore, this question also depends upon the endpoint that is being evaluated and the documents have not provided a basis for either approach. There are huge inconsistencies in the ADME among the PBDEs. Chronic exposure would appear to lead to large body burdens with some of the PBDEs, but not others. Furthermore, simply showing that the compound, a metabolite, or a radiolabel derived from that compound reaches its target site does not establish a causal link. For the developmental effects, in particular, the question of whether levels of the parent compound or a metabolite is the most appropriate dosimeter has to be resolved experimentally, not guessed at. As a start, the variability in the extent of metabolism across these four PBDEs needs to be evaluated to see whether the neurodevelopmental effects appear to occur at similar body burdens of the parent compounds. That is about as far as an analysis could be taken given the data that are available.

The above points are critical as the only compound for which there are cancer data is BDE-209, which appears to be metabolized and excreted much more rapidly than the PBDE's with lower bromine substitution. It does not bioaccumulate to the extent of the other compounds. Therefore, even this chronic effect may not be a function of the body burden. Part of this may have resulted from the lack of context provided for the metabolism & kinetic data that were provided. There are several aspects of the write-ups that suggest that data to this effect may exist, but were simply not critically and/or creatively interpreted or used by the authors of the document. Some of these issues are discussed in greater detail in the editorial comments provided below. To make proper use of the available metabolism and kinetic data that are available requires an integrated assessment of all four compounds. Therefore, one questions why these chemicals are addressed in four separate documents.

Lucio Costa, Ph.D.

Body burden would be an alternative dose metric to derive RfDs, however, current available data are still too limited, in my opinion.

Ralph Kodell, Ph.D.

There are not adequate data for considering body burden as an alternative dose metric to administered dose.

2.2 Do you agree with the rationale described in the Toxicological Review of BDE-99 that the data on the window of susceptibility of the cholinergic receptors to BDE-99 tend to minimize body burden concerns?

Ahmed Ahmed, Ph.D.

Even though I don't completely agree and don't understand clearly the question, I have to accept the concept. That is because any experimental design has to have an assumption that is based on the available information. We know from the literature that the fetal and neonatal brain developments are different in rodents and humans. Therefore, fetal and neonatal cholinergic receptors regulation (up or down) could also be different. While brain development in rodents occurs during postnatal periods, it occurs in utero in humans. Both conditions have extremely different manifestations regarding nutritional, environmental exposure and other toxicokinetic parameters. Therefore, to focus on a specific and certain particular time for susceptibly (PND 3, 7 or 10) for cholinergic receptors in neonates may increase the uncertainty factor in the RFDs' calculation.

Richard Bull, Ph.D.

I am not sure that I understand this question. There is no direct evidence provided that BDE-99 treatment directly affected cholinergic receptors that I could identify in the document. What was presented was an indication that animals treated neonatally with nicotine were responsive to the "loss of habituation" following dosing with BDE-99 at 8 mg/kg at 5 months of age. The effect was not produced by nicotine pretreatment alone, or by only administering BDE-99 at 5 months of age. This is not evidence of an interaction at cholinergic receptors! On the surface, the data obtained with preadministration of nicotine appears to actually separate the mechanism of nicotine from that of BDE-99. The nicotine effects are actually inverted (i.e. suppressed activity) with nicotine at higher doses. Why do neither BDE-99 or nicotine, administered alone, produce the effect when administered at 5 months? The mechanism of the interaction must be complex and indirect.

The second part of the story is that nicotine treatment at PND 10 caused decreases in binding sites for bungarotoxin and QNB, that specifically bind to nicotinic and muscarinic subtypes. A similar effect was observed with BDE-99 administered at PND 10. It is unlikely that the effects of BDE-99 are an expression of an interaction at nicotinic receptors, per se. Binding to such receptors has structural requirements not remotely met by BDE-99 or any of its likely metabolites. Whatever BDE-99 does must involve a less direct mechanism. That could be an inhibition of the expression of these receptors, but just as likely, it could mean that there is a deficit of neurons that express these receptors. If the document goes into mode of action questions, it is imperative that it clearly distinguishes among alternative mechanisms that are possible. One of those criteria clearly has to be a consistency in the doses required to produce the effect and that needed to activate a particular mechanism thought to be a key event in the mode of action. If one mechanism is considered to be more probable, the reasons for this conclusion need to be explicitly stated. Otherwise the document has to conclude that the mechanism of these effects have not been established.

Lucio Costa, Ph.D.

Question is unclear.

Ralph Kodell, Ph.D.

The hypothesis of impaired development of the cholinergic system during the postnatal "brain growth spurt" period as an explanation of the neurobehavioral effects seen in the Eriksson/Viberg studies is plausible. Staskal et al. (2006b) showed that brain levels of BDE-47 administered to neonatal mice on PND 10 were higher than levels in adult animals. Branchi et al. (2002) showed significantly elevated brain levels of BDE-99 in mice administered a high dose from GD 6 to PND 21. Eriksson et al. (2002) also showed that radiolabeled BDE-99 can be taken up and retained in the neonatal mouse brain, although the amount of radioactivity in the brain was only between 0.4% and 0.5% of the administered dose. Viberg et al. (2003b) reported a similar result for BDE-209. The limited data available on BDE-99 indicate that the effects on habituation were seen only at doses that also cause decreased binding of the cholinergic receptor antagonists. For BDE-153, Viberg et al. (2003a) showed that the density of nicotinic acetylcholine receptors in the hippocampus of 6-month old mice treated on PND 10 was significantly decreased at 9.0 mg/kg, a dose at which mice showed significant defects in learning and memory. However, there are no definitive data on mode-of-action. PBDEs have some structural similarity to the thyroid hormone T4. It has been suggested that they may interfere with thyroid hormone transport by competitively binding with one of the transport proteins in plasma. Although it is known that thyroid hormones are essential for normal brain development in humans and that decreases in thyroid hormone levels during fetal and early neonatal life may have profound adverse effects on the developing brain, thyroid hormone levels and behavioral activity were not co-measured in any of the developmental toxicity studies in mice or rats. Although the data on the window of susceptibility of the cholinergic receptors to the PBDEs (PND 3 – PND 10) are suggestive, I believe there are too many other possibilities for mode of action for this rationale to minimize body-burden concerns.

3. QUESTIONS RELATED TO THE CARCINOGENICITY ASSESSMENT OF BDE-209

3.1 Is the weight of evidence for the carcinogenicity of BDE-209 in the draft Toxicological Review appropriately described? Are there additional studies that should be included?

Ahmed Ahmed, Ph.D.

The weight of evidence on the carcinogenicity of BDE 209 in the draft toxicological review is based on a carcinogenicity studies that were conducted more that quarter of a century ago. Although the authors of the draft review document have provide a methodical and complete description of the studies, the study itself and its results leave a lot to be desired. Modern, molecular and more sensitive biomarkers of cancer should be implemented in future carcinogenesis studies for BDE-209 and other congeners. The current available studies had shed some doubts regarding the pre-carcinogenic effects of BDE 209. The studies utilized very high doses which lead to some toxic effects and increased animal deaths.

Currently I am not aware of any recent study that addressed the carcinogenicity of BDE-209.

Richard Bull, Ph.D.

Yes.

Lucio Costa, Ph.D.

The weight of evidence for carcinogenicity of BDE-209 is appropriately described. I am not aware of any additional studies.

Ralph Kodell, Ph.D.

The weight of evidence for the carcinogenicity of BDE-209 is appropriately described. I do not know of additional studies that should be included.

3.2 Do the data support estimation of a cancer slope factor for BDE-209? If yes, is the rationale for the quantitative analysis objectively and transparently described, considering the uncertainty in the data and the suggestive nature of the weight of evidence? Have the rationale and justification for the use of linear low-dose extrapolation been objectively and transparently presented?

Ahmed Ahmed, Ph.D.

The available data supports the estimation of a cancer slope factor for BDE-209. The rationale for the qualitative analysis was objectively and transparently described. Similarly the justifications for the use of linear low dose extrapolation have been objectively presented.

Richard Bull, Ph.D.

After reading the public comments directed at treatment of the carcinogenesis data that is available on BDE-209, it is apparent that there are a variety of problems with the NTP data. Comments from industry focused on the fact that the responses were fairly modest and that the criteria have changed for classifying liver lesions in the rat since this study was completed. I am less concerned with the scoring nodules as tumors. Nodules generated in initiation promotion protocols are known to regress with suspension of treatment. This is much less likely to happen with chronic studies of a single compound.

However, I question the appropriateness of the original NTP study for developing risk estimates in general. The very high concentrations were provided to the animals in the diet make it almost certain that the external dose is not a reliable indication of the systemic dose. The extremely low solubility of BDE-209 in aqueous media (<0.1 ug/L) suggests that the transfer rate from food to aqueous phase would sharply limit to absorption proportional to external dose to much lower concentrations than the 25,000 and 25,000 ppm in the diets used in the NTP study. The document contains data indicating that absorption is sharply curtailed at much lower concentrations in the diet (see quotation of studies of El Dareer et al., 1987) and the fact that much higher percentages of absorption were derived from the gavage dosing of much smaller doses of PBDE-209 (see Sandholm et al. 2003; Morck et al. 2003). These observations are supported by the more uncertain studies of the absorption of the labeled compound. While there were some evidence of tumor induction in both mouse and rat studies, there was little indication of dose-response, suggesting that the response was limited by absorption. If this is the case, the true point of departure for estimating cancer risk could be order of magnitude lower than is suggested by the doses administered. For this reason, revisiting the results of the NTP studies will be a waste of time and money. I would strongly suggest that a new bioassay be conducted that can be more easily related to environmental exposures. The doses administered in such studies should be established based on better designed studies of absorption, distribution and metabolism than have been conducted to date and development of a first generation PBPK model.

Lucio Costa, Ph.D.

Data are indeed suggestive of a carcinogenic potential of BDE-209. BDE-209 does not appear to be genotoxic (though database is limited), but no clear indication of possible epigenetic mechanism is available. On the other hand, chronic toxicity studies suggest the induction of non neoplastic or pre-neoplastic lesions in target organs. The linear low dose extrapolation as a default, conservative approach appears justified in this case, as is the classification of BDE-209 as a possible human carcinogen.

Ralph Kodell, Ph.D.

The data appear to support estimation of a cancer slope factor for BDE-209 based on neoplastic nodules or carcinomas (combined) in the livers of male rats (NTP, 1986). This conclusion assumes that any change in the classification of neoplastic nodules that might have taken place subsequently would not change the dose-response appreciably. The rationale for the quantitative analysis is transparently described. The cancer data are characterized as providing "suggestive evidence of carcinogenic potential," in keeping with the EPA cancer guidelines (EPA, 2005a). The modeling of several tumorigenic endpoints leads to selection of the cancer slope factor corresponding to the most sensitive endpoint (liver nodules/carcinomas). I did not see a rationale or justification for the use of linear low-dose extrapolation, except for a reference (page 62) to two EPA guidelines documents for cancer assessment (EPA, 2005a, 2005b).

3.3 Are there alternative modeling approaches that should have been considered instead of or in addition to the linear low-dose extrapolation approach?

Ahmed Ahmed, Ph.D.

To my knowledge the authors have explained all possible modeling approaches. They selected the best fit model for their interpretation of the experimental data. I commend the authors' consciousness for siting the drawbacks of these studies and for the thorough analysis of the available data.

Richard Bull, Ph.D.

There are no data that would permit departure from linear low-dose extrapolation. As indicated above, I am concerned about the very high doses that were used in these studies. It is not clear that absorption would be linear with dose because of the solubility problems that are discussed in more detail in the editorial comments that have been appended to these responses to EPA's specific questions.

Lucio Costa, Ph.D.

Data are indeed suggestive of a carcinogenic potential of BDE-209. BDE-209 does not appear to be genotoxic (though database is limited), but no clear indication of possible epigenetic mechanism is available. On the other hand, chronic toxicity studies suggest the induction of non neoplastic or pre-neoplastic lesions in target organs. The linear low dose extrapolation as a default, conservative approach appears justified in this case, as is the classification of BDE-209 as a possible human carcinogen.

Ralph Kodell, Ph.D.

Other modeling approaches could have been considered, but I don't think that they necessarily should have been considered. The liver dose-response data are quite linear and there are only two nonzero doses plus a zero-dose control. The linear model fits quite well. It seems likely that other dose-response models would give similar fits. It's possible that such models would extrapolate differently from the linear model below the data, but it is my opinion that the data themselves are not informative enough to justify a different, say, sub-linear, extrapolation approach.

MISCELLANEOUS REVIEWER COMMENTS

Ahmed Ahmed, Ph.D.

Comments on Each Document:

BDE 47:

1. Page 7; 3.2.1: Current Human data regarding distribution and disposition of BDE 47 is spotty, sporadic with low number of samples and uncontrolled health and environmental conditions, with no regard to geographical or ecological circumstances.

2. Human data should be summarized and presented in a comprehensive table with references in this and in all other documents.

3. Page 13; 3.2.2: Animal data on the disposition of BDE-47 focused on several 14C labeled compounds. In most of these studies, the position of the label was not mentioned, the purity of the 14C-compound was not known, the specific activity of the compound was not given and the ADME studies were based on following the radioactivity in various tissues and biological media. No pharmacokinetic parameters were estimated from these studies.

4. The identity of the detected radio labeled species in tissues and biological fluids is very important to clarify whether this species is the parent molecule, a metabolite or even a carbon dioxide molecule.

5. The levels of radioactivity should be uniformly expressed throughout this document and other documents. That is essential to be able to do reasonable comparisons among various congeners. Concentrations as mg-equivalent / g tissue/g lipid weight should be used across the document.

6. I suggest that the authors to put some proposed metabolic pathways for this compound. It could be extracted from other brominated congeners such as BDE-99. The proposed metabolic pathway similar to that presented for BDE-99 could be used here too. This will strengthen the fact that this and other lower brominated congeners could be obtained from higher brominated ones.

Mice are known to have higher levels of various CYT P450 enzyme activities than rats. This should be reflected in the discussion of the differences in the disposition, metabolism and excretion of this compound and other congeners.

8. Extensive explanation of receptor site interaction is somewhat confusing due to the lackluster effects of these compounds on various receptors. It would be beneficial if a summary table is presented either in the beginning or at the end of this section. Relative potency of various congeners on specific receptors should be indicated.

9. A table, in page 39, that could summarize the neurobehavioral, developmental and reproductive effects of BDE-47 should be added. It will show how Eriksson et al represent as complete a study to be used in RFD determination. It will be helpful if in each document a similar table is inserted before the selection of the principal study as in case of the document of BDE-99.

10. The Uncertainty Factors for population at risk (fetuses and newborn) and for conversion from single dose to multiple and continuous routes of exposure should be adjusted for, as described before.

11. The neurobehavioral studies that are utilized in RFD evaluation have limited end points and were conducted in one Swedish research location. Due to the lack of complete dose response/ time course studies, I have to agree on using them in the determination of the corresponding RFD. My agreement is based on the fact that these studies have statistically significant end points for neurobehavioral adverse effects within the framework of the experimental design.

12. A major concern about the experimental design, described in these studies, is ignoring the "letter effect". The authors of the study should have used offspring from multiple letters rather than from one letter. Randomization was based on only two letter and randomization approach was not described.

13. Although radioactivity was detected in brain, in the studies, there was no explanation in which brain areas radio activity was detected. Anatomical or histological localization of the radioactivity would have added significant weight to the mechanisms of the observed neurobehavioral studies.

14. There seems to be no correlation between the postnatal day of exposure and the concentration in the brain. Exposure at PN Day 10 provided the brain with the highest concentration while had no increase in neurobehavioral adverse effect.

BDE-99

1. The table in page 58 is an excellent summary to the developmental and reproductive effects of several BDEs. It shows how Viberg et al (2004a) represent as complete a study to be used in RFD determination. It will be helpful if in each document a similar table is inserted before the selection of the principal study for RFD estimation.

2. Study of Kuriyama et al (2005) showed some good dose-response relationship for neurobehavioral as well as male reproductive effects. This study should be considered in the determination of RFD for BDE-99.

3. ADME evaluations in animals are un-objectively presented. They were presented as several summaries of several studies but with no connection and with limited interpretations of the data. The proposed metabolic pathway presented in page19 is very helpful. Similar pathway should be presented for other congeners.

4. Due to the metabolic relationship between higher and lower congeners of BDE, a comprehensive metabolic profile for all of these compounds should be presented in every toxicological review for each individual BDE.

5. Comments on the radioactive compound, its purity and specific activity that are described before, will also apply for this and every other congener.

6. There are large number of receptor studies that are presented in the document. A comparative summary with references will be helpful for the reader to easily conclude which is the most sensitive receptor for this and other congeners.

7. Concerns regarding Uncertainty Factors described before, apply here, too, for BDE-99.

BDE-153

1. Human distribution studies are somewhat sporadic and most of them were designed for the detection of other chemicals. The data in table 5 should be expanded to include BDE- 209. This table should be presented in the document of every congener.

2. I would suggest that the authors of the document should create a summary of values for the concentration of various PBDs in human tissues in various geographic locations. Schecter et al (2003) showed that the mean median concentrations of BDE in Texas are much higher than any other places in USA or Europe.

3. A summary table for receptor studies is needed.

4. Comments about 14C ADME studies described before apply here too.

5. Need to insert comprehensive metabolic pathway similar to that in BDE-99 document.

6. In most of the in vitro and in vivo animal studies that are presented in these documents, oily vehicles were used (corn oil etc.). I found this problematic. That is because large number of bromine atoms on a phenyl ring imparts several electrophillic and lipophilic properties to the aromatic ring. The increased lipophilicity will significantly alters the distribution and tissue uptake of BDE between the oily vehicle and the biological system with its hydrophilic / lipophilic properties. These conditions lead to decreased absorption and distribution with subsequent alteration in metabolism and excretion with little correlation to real occupational and environmental conditions.

7. Rational for driving RDF and Conclusions are appropriate and transparently presented. A summary table for all available studies that could be used for the estimation of RFDs should be included. This table will clarify why a particular study was the most appropriate for the estimation of RFD.

BDE-209

1. The cancer risk derived for BDE-209 is based on very high doses utilized in a two and half decade old study. These doses could not be occupationally or environmentally possible except in accidental conditions.

2. Like other toxicological reviews of other BDEs, ADME evaluations in animals are un-objectively presented. There are several summaries of several studies but no connection and limited interpretations of the data. The proposed metabolic pathway presented in for BDE-99 is very helpful. Similar pathway should be presented for this and other congeners.

3. Due to the conversion of higher molecular weight BDEs (those with larger numbers of bromine atoms) metabolic relationship between higher and lower congeners of BDE exists. Therefore, a comprehensive metabolic profile of all these compound should be presented in every toxicological review for each individual BDE.

4. Comments on the radioactive compound, its purity and specific activity that are described before, apply for this and every other congener.

5. Extensive number of receptor studies is presented in the document. A comparative summary with references will be helpful for the reader to easily conclude which is the most sensitive receptor for this congener (and other ones).

6. Concerns regarding Uncertainty Factors described before, apply here for BDE-209, too.

Richard Bull, Ph.D.

Editorial comments:

1. The Agency should reconsider the traditional organization of these review documents. The old organization is becoming very cumbersome as more and more data become available that bear on the issue of mode of action or corroborating data that support the documents overall

conclusions. In this particular set of documents, the artificial separation of the neurobehavioral studies and neurochemical data over three categories (reproductive/developmental studies, neurotoxicity and Other studies) really made these difficult documents to review. I suggest that all of the data that contribute to a cohesive understanding of a particular toxicological effect need to be included in the same section. To pick a specific case, all data relevant to the neurodevelopmental effects of BDE-99 should be presented together, whether the data relate to neurobehavioral, neurochemical, or gene expression data in the CNS.

Related to this point, it is also suggested that conclusions that are derived from explorations of alternative modes of action for a particular effect be expressed more categorically. For example, there have been some investigation of contribution of thyroid hormones changes to the neurodevelopmental effects of the BPDEs. The only clear results with respect to the thyroid hormones is that of Zhou et al (2002), where effects of a different mixture (DE-71, a mixture of tetra and penta PBDEs) on thyroid hormone levels were described. The doses required to produce such effects were not far off those that produced neurodevelopmental effects with BDE-47, but were much higher that the doses of PDE-99 that produced neurodevelopmental effects. Thyroid hormone levels were examined in a study of adults treated with BDE-47 by Hallgren and Darnerud (2002), but only FT4 was reduced, not thyroxine, and the dose required to produce this effect was much too high. Other studies with the PBDEs appear to be negative, but in some cases the actual doses utilized were not provided in the document (e.g. the Hakk et al. 2002 study cited in the BDE-99 document). To this reviewer there is no basis for suggesting that the neurodevelopmental effects observed with the PBDEs are related to thyroid hormone-related effects. This actually raises concerns, rather than lowering them. If a thyroid hormone-based mode of action were identified, there would be less of concern because the risks associated with this mode of action are reasonably well understood. Therefore, a clear conclusion should be drawn that says it appears unlikely that modified thyroid function plays a role in the neurodevelopmental effects observed with this class of compounds. Similar statements should address other modes of action that have been found to be consistent with or inconsistent with respect to particular toxicological effects. In the absence of a particular toxicological effect, these data are of little use. It is really important to begin to make these distinctions as the "presumed mode of action data" may frequently form the bulk of the available data on a compound and this information needs to be placed into better context.

2. The data on PBDE occurrence in biological samples involve relatively small populations and may not be representative of either the U.S. or the World populations. Nevertheless, there are observations that imply an evolution of exposures that are somewhat different in the U.S. and other parts of the world. Similarly, there appears to be a pattern of exposures, reflected in tissue measurements, that is increasing in recent years (presumably because of the recent introduction of these compounds in new industries). These are important issues and need to be presented more proactively – i.e. in a way that supports or denies these apparent trends in exposure and providing a specific a basis for these observations, if true. As the section now stands, it simply iterates studies in a more or less sequential way, providing some casual notion of the existence of these patterns, but not really determining whether the databases are strong and representative enough to support these conjectures or not. A few specific comments, drawn largely from the BDE-47 document as much of this information is repeated in the subsequent documents, which illustrate the problematic nature of some the discussions that were provided in the document are provided below:

a. There are several places in the discussion of data obtained with 14C that need to be clarified. Either the document poorly explains the nature of the data that is summarized or it has been misinterpreted. One example of a problem in interpretations of greater concentrations of 14C in tissues following a series of doses of non-radiolabeled compound. Such observations are frequently the result of isotope effects (e.g. the prior exposure results in a tissue pool of compound in tissues that is significantly larger than in control animals. As a result more isotope remains in the tissue pools as it becomes diluted in specific activity). The document suggests that these data reflect is a magnification of amounts of chemical that is retained with subsequent doses. This is unlikely. The only way this can be dealt with quantitatively is if the specific activity of the chemical is determined in each tissue for the single dose without prior treatment vs. that observed with a dose after prior treatment with non-labeled chemical.

b. The frequent suggestion that a smaller fraction of dose was absorbed with increasing dose as evidence of saturable absorption may also be inappropriate. There are other possibilities that have to be entertained. In the case of compounds with chemicals of such limited water solubility, such observations may well be explained by limited access to membranes because of low solubility and, more important, the limited solubility in body fluids to carry away the compound from its site of application. The solubilities of these compounds in water are listed as BDE-47 = 11 µg/L; BDE-99 =2.4 µg/L, BDE-209 = <0.1 µg/L, BDE = 0.9 µg/L. The Hughes et al. 2001 study of passage of BDE-209 through mouse skin in vitro would be plagued by this problem unless a perfusion system was used (not stated in the document). Incidentally, the doses applied in this preparation were given in amounts, not concentrations. It is essential to know concentrations to interpret these in vitro studies. The limited solubility could even affect the data obtained with 14C-labeled compounds (e.g. Viberg et al.) because these generally much smaller doses (e.g. 2.2 mg/kg) still exceed the solubility in water by a 4 orders of magnitude in the case of BDE-209. The authors of the papers reviewed may have addressed these issues, but it did not come through in the Toxicological Reviews.

The in vivo studies that employed huge concentrations in the diet would certainly have the same problem. In fact, one wonders whether the lack of clear dose-response in the NTP study of BDE-209 might reflect this problem. Equivalent responses may have been observed at much lower doses. In my view this is a real concern for estimating cancer risk from these data.

3. It is nice to have a reasonably complete discussion of the metabolism of the PDBEs in the IRIS documents. Nevertheless, there is a need to address some confusing aspects of the discussions of uptake, metabolism, distribution, and elimination of compounds in these documents rather than simply reiterating the results. One way of reducing the confusion might be a summary at the beginning of this section that lays out what appears to be happening, even to providing the conclusions of the section up front. This would avoid being surprised by the apparent finding that urinary elimination in mice, for example, appears dependent upon binding of the parent compound to a urinary protein at the end. As the descriptions are laid out, the reader is continuously struck by what appears to be results that appear contrary to general rules (e.g. that non-polar compounds are not efficiently eliminated in the urine).

There are differences among studies related to the apparent extent of metabolism of the compounds and the extent to which metabolites occur in the excreta that are presented without comment. If at all possible, this issue should be driven to conclusions that are useful in making judgments related to how harmful these compounds are. If the information is not useful or conclusions cannot be drawn, this should be stated and the presentation of this material substantially shortened.

Part of the confusion arises from the apparent reliance on measurement of 14C in these studies. These measurements are intermixed with some direct chemical measures, but that is frequently not made clear in the Toxicological Reviews. While these sections read well and are unlikely to be questioned by a casual reader, the informed reader immediately gets distracted by the methodological questions and feels that the apparent conclusions require challenge. Furthermore, questions of metabolism, covalent binding, and distribution are not possible simply by measuring the 14C.

Some specific points in the text of the BDE-47 document are referred to below where the interpretation of ADME data is ambiguous are provided below:

p. 14, 3rd para. This is an example where the legitimacy of the interpretation that there are different amounts absorbed from a dose of radio-labeled compound was administered on day 1 vs. after 10 days of administration of non-labeled compound needs to be questioned.

p. 17, second para in after Metabolism title. The last two sentences appear contradictory.

p. 17, last para. How is "covalently bound" defined (or measured)?

P. 18, 2nd full para. These results for the last day are likely to reflect accumulated metabolites from the prior exposures. Therefore, it is inappropriate to compare the amount of metabolite observed after day 1 to day 10.

p.22, 2nd par. Fifth line. It is not clear where the half-life is being measured. Was it actually in the perirenal fat or was it in the blood? The writing implies that it is in the perirenal fat but the wording is not definitive. This needs to be very clearly stated as most half-life measures are made in blood and that half-life is used to predict turnover in tissues that are sinks (e.g. fat).

Lucio Costa, Ph.D.
Additional comments

BDE-47

p. 9 Discussion on levels in human milk could be expanded.

p. 17 It is unclear why uptake of BDE-47 in cultured neuronal cells in the presence of 10% horse serum "is likely to be more representative of in vivo conditions".

p. 39 It is unclear why data on exposure to BDE-47 in relationship to thyroid hormone levels cannot be used for deriving RfD. The study of Hallgren and Darnerud provides a NOAEL of 6 mg/kg/day and a LOAEL of 18 mg/kg/day. Changes in mixed function oxidase system that were observed at 6 mg/kg/day may be discounted, as suggested.

p. 40 The important issue of pup vs. litter as the statistical unit is discussed, with the indication that the use of more than one pup/litter in the Eriksson et al., 2002 study may bias the results. Yet, in the footnote, a study by Eriksson et al., 2005 (only in abstract form) with BDE-99 is discussed, in which this same issue was shown not to influence the outcome. Perhaps this should be integrated in the main text.

p. 41 An UF of 3 for single vs. chronic exposure may not be necessary. The concept of "windows of susceptibility" during brain development would argue that chronic exposure may not necessarily result in greater adverse effects, but rather that even a single exposure at a specific sensitive time-point may elicit the highest effect. Eriksson et al. have shown with other compounds (e.g. BDE-99) that a single exposure on PND10 is the most sensitive time point. This comment would apply to other BDEs as well.

BDE-99

p. 29 Data on nicotinic receptor changes from the Viberg et al. 2004b study could be presented here. Refer here to data on p. 49.

p. 46 Here and elsewhere, when referring to Casarett and Doull's Toxicology textbook, the most recent edition (2001) could be used.

p. 48 Better references than Klaassen, 1996 or Ankenberg, 2003 could be used to discuss distribution and functions of cholinergic receptors.

p. 48 Discussion of the Ankenberg, 2003 study could be shortened, as it is not of much relevance. It is also presented unclearly.

p. 49 Choose reference other than Klaassen 1996, to indicate effects of atropine. Also, specify % decrease of 3H-QNB binding.

p. 51 Section 4.4.3 (neurotoxicity) should be renamed, as several previous sections (e.g 4.3.1, 4.3.2) already deal with developmental neurotoxicity. Eriksson is also a co-author of the proteomics paper by Alm et al. discussed here.

p. 53 Additional in vitro mechanistic experiments (see references above) may be added here and in section 4.5.3 on mode of action.

p. 56 Data on oxidative stress and BDEs (see references above) may be added here.

p. 57 In section 4.7.2 the reference Branchi et al. 2002 may be added to indicate lack of gender-specific effects.

p. 65 Use of an UF of 3 for extrapolation from subchronic to chronic may not be necessary (see comment for BDE-47). Also, given the availability of several developmental neurotoxicity data on BDE-99, an UF of 10 for database uncertainty seems excessive.

p. 68 The overall confidence in the RfD determined for BDE-99 is listed as low, same as in case of BDE-47. However, given the existence of multiple studies corroborating the main conclusions, confidence level may be raised to moderate.

BDE-153

p. 18 The % decrease of nicotinic receptors in the study by Viberg et al. 2003a could be indicated (see p. 23).

p. 28 UF of 3 for subchronic to chronic may not be necessary (see comments for BDE-47).

BDE-209

p. 12 The possible debromination of BDE-209 to lower bromine congeners may be better discussed, if possible. Should also environmental debromination be mentioned?

p. 16 Half-life may not be necessarily directly linked to rapid metabolism.

p. 38 Content of section 4.5.1 is not in tune with title of section.

p. 58 An UF (e.g. 3) for deficient available database may be added. While, differently from other BDEs, studies are available on subchronic, chronic and developmental toxicity (all yielding NOAELs or BMDs substantially higher than that from the stuies of Viberg et al), no other developmental neurotoxicity evidence is available.

Report is at times repetitive, and could be shortened. For example, results of the Viberg et al. 2003a study are described on p. 10, 33-34, 41-42, 50 and 53.

Ralph Kodell, Ph.D.

Miscellaneous comments

General

The presentation of the data and the derivation of RfDs might benefit from a unified presentation in a single document, instead of four separate documents. In particular, similarities and differences in ADME could be addressed in a cohesive manner.

Specific

BDE-47

Section 3.1, last sentence: It seems that the relative absorption rates of rats and mice are not qualitatively the same in the two studies compared, contrary to what is stated.

Page A-2: The AIC is highest for the selected linear model, which fits best in terms of the p-value. For BDE-209, page A-10, low AIC seems to be one of the selection criteria, along with high p-value. I believe the selection criteria should be consistent. AIC is sometimes used as a weight for averaging the results of several models. It might be a better criterion than p-value.

Page A-2: The indication is that modeling was done for both males and females. But, there were no female data.

BDE-99

Page 81: The Hill model fits best in terms of its having the highest p-value. However, it also has ~~the highest AIC. This isn't consistent with BDE-209, where low AIC is one of the criteria for~~ model selection. AIC should be used consistently.

BDE-209

Page 21: How can 99 mg/kg-day be characterized as a NOAEL in the study by Carlson (1980) when it was associated with a statistically significant increase in the liver-to-body-weight ratio? (Same in Table 2, page 19)

Page 32, lines 5-8: I strongly disagree with the conclusion by Eriksson et al. (2005) regarding litter-based studies. This sentence should be re-stated so that it doesn't sound like this conclusion is accepted as fact by EPA. In general, this conclusion is erroneous.

Page 34, lines 13-15: There is something wrong with the sentence. A decrease in disruption of habituation is not an adverse effect.

Page 38, lines 6-3 from bottom: There is something wrong with this sentence. Thyroid tumors were seen in females as well as males, but they were not significant in either sex. Why is NTP (1984) cited?

Page 39, lines 12-11 from bottom: There is the same problem regarding the statement about thyroid tumo

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TOXICOLOGICAL REVIEW

OF

DECABROMODIPHENYL ETHER
(BDE-209)

(CAS No. 1163-19-5)

In Support of Summary Information on the
Integrated Risk Information System (IRIS)

June 2008

U.S. Environmental Protection Agency
Washington, DC

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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LIST OF ACRONYMS

AhR	aryl hydrocarbon receptor
AIC	Akaike Information Criterion
ALH	amplitude of the lateral head displacement
ATSDR	Agency for Toxic Substances and Disease Registry
AUC	area under the curve
BDE-209	decabromodiphenyl ether
bDNA	branched deoxyribonucleic acid
BMD	benchmark dose
BMDL	BMD 95% lower bound
BMDS	benchmark dose software
BMR	benchmark response
CALUX	Chemical-Activated LUciferase eXpression
CAR	constitutive androstane receptor
CASRN	Chemical Abstracts Service Registry Number
CD25	interleukin-2-receptor α chain
cDNA	complementary DNA
C_{max}	maximum concentration
CYP-450	cytochrome P-450
decaBDE	decabromodiphenyl ether
DRE	dioxin-responsive element
E2	17β-estradiol
ED	effective dose
ER	estrogen receptor
EROD	ethoxyresorufin O-deethylase
FOB	functional observational battery
fw	fresh weight
GC/MS	gas chromatography/mass spectrometry
HED	human equivalent dose
hexaBDE	hexabromodiphenyl ether
i.v.	intravenous
IRIS	Integrated Risk Information System
LED	95% lower confidence limit for the effective dose
LOAEL	lowest-observed-adverse-effect level
lw	lipid weight
MMP	mitochondrial membrane potential
MRL	minimal risk level
mRNA	messenger ribonucleic acid
NAS	National Academy of Science
NOAEL	no-observed-adverse-effect level
nonaBDE	nonabromodiphenyl ether
NTP	National Toxicology Program

octaBDE	octabromodiphenyl ether
PBDE	polybrominated diphenyl ether
PBPK	physiologically based pharmacokinetic
PCB	polychlorinated biphenyl
pentaBDE	pentabromodiphenyl ether
PND	postnatal day
PROD	pentoxyresorufin O-deethylase
PXR	pregnane X receptor
RfC	reference concentration
RfD	reference dose
RSD	risk-specific dose
SXR	steroid X receptor
T_3	triiodothyronine
T_4	thyroxine
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
tetraBDE	tetrabromodiphenyl ether
triBDE	tribromodiphenyl ether
TSH	thyroid stimulating hormone
UDPGT	uridine diphosphate glucuronyl transferase
UF	uncertainty factor

FOREWORD

The purpose of this Toxicological Review is to provide scientific support and rationale for the hazard and dose-response assessment in IRIS pertaining to chronic exposure to decabromodiphenyl ether. It is not intended to be a comprehensive treatise on the chemical or toxicological nature of decabromodiphenyl ether (BDE-209).

This health assessment deals with BDE-209 of relatively high purity (≥94%) and does not deal with earlier commercial decabromodiphenyl ether mixtures containing lower proportions of decabromodiphenyl ether (e.g., 75% purity). In addition to BDE-209, IRIS health assessments have also been prepared for three other polybrominated diphenyl ether congeners: tetraBDE-47, pentaBDE-99, and hexaBDE-153. These four congeners are those for which toxicological studies suitable for dose-response assessments were available and are the ones most commonly found in the environment and human biological media.

The intent of Section 6, *Major Conclusions in the Characterization of Hazard and Dose Response*, is to present the major conclulsions reached in the derivation of the reference dose, reference concentration and cancer assessment, where applicable, and to characterize the overall confidence in the quantitative and qualitative aspects of hazard and dose response by addressing the quality of data and related uncertainties. The discussion is intended to convey the limitations of the assessment and to aid and guide the risk assessor in the ensuing steps of the risk assessment process.

For other general information about this assessment or other questions relating to IRIS, the reader is referred to EPA's IRIS Hotline at (202) 566-1676 (phone), (202) 566-1749 (fax), or hotline.iris@epa.gov (email address).

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This document has been reviewed by EPA scientists, interagency reviewers from other federal agencies, and the public, and peer reviewed by independent scientists external to EPA. A summary and EPA's disposition of the comments received from the independent external peer reviewers and from the public is included in Appendix A of the Toxicological Review of 2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether (BDE-209).

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1. INTRODUCTION

This document presents background information and justification for the Integrated Risk Information System (IRIS) Summary of the hazard and dose-response assessment of 2,2',3,3',4,4',5,5',6,6'-decabromodiphenyl ether (BDE-209). IRIS Summaries may include oral reference dose (RfD) and inhalation reference concentration (RfC) values for chronic and other exposure durations, and a carcinogenicity assessment.

The RfD and RfC, if derived, provide quantitative information for use in risk assessments for health effects known or assumed to be produced through a nonlinear (presumed threshold) mode of action. The RfD (expressed in units of mg/kg-day) is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The inhalation RfC (expressed in units of mg/m^3) is analogous to the oral RfD, but provides a continuous inhalation exposure estimate. The inhalation RfC considers toxic effects for both the respiratory system (portal of entry) and for effects peripheral to the respiratory system (extrarespiratory or systemic effects). Reference values are generally derived for chronic exposures (up to a lifetime), but may also be derived for acute (≤24 hours), short-term (>24 hours up to 30 days), and subchronic (>30 days up to 10% of lifetime) exposure durations, all of which are derived based on an assumption of continuous exposure throughout the duration specified. Unless specified otherwise, the RfD and RfC are derived for chronic exposure duration.

The carcinogenicity assessment provides information on the carcinogenic hazard potential of the substance in question and quantitative estimates of risk from oral and inhalation exposure may be derived. The information includes a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen and the conditions under which the carcinogenic effects may be expressed. Quantitative risk estimates are derived from the application of a low-dose extrapolation procedure. If derived, the oral slope factor is a plausible upper bound on the estimate of risk per mg/kg-day of oral exposure. Similarly, an inhalation unit risk is a plausible upper bound on the estimate of risk per µg/m^3 air breathed.

Development of these hazard identification and dose-response assessments for BDE-209 has followed the general guidelines for risk assessment as set forth by the National Research Council (1983). EPA guidelines and Risk Assessment Forum Technical Panel Reports that may have been used in the development of this assessment include the following: *Guidelines for the Health Risk Assessment of Chemical Mixtures (U.S. EPA, 1986a), Guidelines for Mutagenicity Risk Assessment* (U.S. EPA, 1986b), *Recommendations for and Documentation of Biological Values for Use in Risk Assessment* (U.S. EPA, 1988), *Guidelines for Developmental Toxicity*

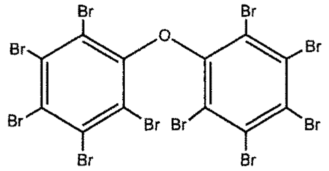
Risk Assessment (U.S. EPA, 1991), *Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity* (U.S. EPA, 1994a), *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (U.S. EPA, 1994b), *Use of the Benchmark Dose Approach in Health Risk Assessment* (U.S. EPA, 1995), *Guidelines for Reproductive Toxicity Risk Assessment* (U.S. EPA, 1996), *Guidelines for Neurotoxicity Risk Assessment* (U.S. EPA, 1998), *Science Policy Council Handbook: Risk Characterization* (U.S. EPA, 2000a), *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2000b), *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 2000c), *A Review of the Reference Dose and Reference Concentration Processes* (U.S. EPA, 2002), *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a), *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005b), *Science Policy Council Handbook: Peer Review* (U.S. EPA, 2006a), and *A Framework for Assessing Health Risks of Environmental Exposures to Children* (U.S. EPA, 2006b).

The literature search strategy employed for this compound was based on the Chemical Abstracts Service Registry Number (CASRN) and at least one common name. Any pertinent scientific information submitted by the public to the IRIS Submission Desk was also considered in the development of this document. The relevant literature was reviewed through November 2007.

2. CHEMICAL AND PHYSICAL INFORMATION

Decabromodiphenyl ether (decaBDE or BDE-209) is a fully brominated diphenyl ether compound (i.e., 10 bromine atoms) used as a flame retardant. The composition of commercial decaBDE is almost exclusively the deca-substituted BDE-209 (typically ≥97%), the remainder being nonabromodiphenyl ether (nonaBDE); trace amounts of octabromodiphenyl ether (octaBDE) may be present (Schecter et al., 2003; American Chemistry Council, 2002; Hardy, 2002). The composition of older decaBDE formulations, which are no longer commercially produced in the U.S., was approximately 77% decaBDE, 22% nonaBDE, and 1% octaBDE (Kociba et al., 1975). Physical and chemical properties of decaBDE (≥97% purity) are listed in Table 2-1.

Table 2-1. Physical properties and chemical identity of decaBDE

	Physical property/chemical identity	Reference
CASRN	1163-19-5	U.S. EPA (2004)
Synonyms	2,2',3,3',4,4',5,5',6,6'-decaBDE; BDE-209; decaBDE; benzene, 1,1'-oxybis[2,3,4,5,6,-pentabromo]-; decabromodiphenyl oxide; decabromodiphenyl ether; decabromobiphenyl ether; ether, bis(pentabromophenyl)	U.S. EPA (2004); ATSDR[a] (2004)
Physical state	Solid	Hardy (2002)
Melting point, °C	300–310	ECB[a] (2003)
Boiling point, °C	decomposes at >320°C	ECB (2003)
Vapor pressure at 21°C, Pa	4.63×10^{-6}	Hardy (2002)
Henry's law constant: atm m^3/mol (Pa m^3 mol^{-1}) at 25°C	 1.93×10^{-8} 0.04	Hardy (2002); Cetin and Odabasi (2005)
Density, g/cm^3	3.0	NAS[a] (2000)
Water solubility at 25°C, µg/L	<0.1	Hardy (2002)
Log K_{ow}	6.3–12.6	Hardy (2002)
Log K_{oc}	6.3	Hardy (2002)
Molecular weight	959.17	U.S. EPA (2004)
Chemical formula	$C_{12}Br_{10}O$	U.S. EPA (2004)
Chemical structure	 Br Br O Br Br Br Br Br Br Br Br	

[a]ATSDR = Agency for Toxic Substances and Disease Registry; ECB = European Chemicals Bureau; NAS = National Academy of Science.

3. TOXICOKINETICS

Data on the toxicokinetics of decaBDE in humans are limited to findings on the levels in serum and maternal milk that demonstrate it is absorbed from the environment and distributed to tissues. Several studies have been conducted to evaluate the absorption, distribution, metabolism, and elimination of decaBDE after oral or intravenous (i.v.) dosing in rats and mice. Absorption is low (7–26%) after oral exposure to rats. Following absorption, the highest levels are found in the liver, muscle, and skin. This differs from studies of the lower brominated congeners, where the highest levels are generally found in the adipose tissues. The available metabolic data apply exclusively to rats, where both debrominated and hydroxylated-debrominated species have been identified in plasma. In one study, the metabolites in the feces exceeded those that could be accounted for from bile, raising the possibility that some conversion of the parent compound may be mediated by the intestinal epithelium or microflora. This phenomenon was not reported for the lower brominated BDE congeners. Urinary excretion of decaBDE-209 is minimal in rats; no data are available for mice. In rats, some of the urinary radiolabel (18%) was bound to albumin.

3.1. ABSORPTION

3.1.1. Studies in Humans

There are no direct studies of decaBDE absorption in humans. The data that demonstrate human absorption come from measurements of decaBDE in human biological media after anthropogenic exposures but do not provide information on the quantitative aspects of absorption or the kinetics of tissue distribution and retention.

3.1.2. Studies in Animals

Studies on BDE-209 absorption following oral dosing demonstrate its absorption potential. However, there were few direct measurements of absorbed dose, and absorption estimates are based on a combination of concentrations in blood and data on excretion. Among the several oral dosing studies, the percentage of an administered dose absorbed across the gastrointestinal tract ranged from approximately 7–26%. In some cases it was difficult to derive an accurate estimate of absorption because of the high proportion of the dose found in the feces (>90%) and the high percentage that was present as metabolites in feces.

Sandholm et al. (2003) evaluated the bioavailability of unlabeled decaBDE in male Sprague-Dawley rats. One group of rats (n = 18) was dosed by gavage with unlabeled decaBDE (>98% purity) in dimethylamide/polyethylene glycol/water vehicle at 2 µmol/kg (1.9 mg/kg). Another group of rats (n = 18) was dosed intravenously via the tail vein with unlabeled decaBDE at the same dose. At specific time intervals, blood samples from three rats per group were collected according to the following schedule: group 1 was sampled 1 hour and 24 hours after dosing; group 2 after 3 hours and 48 hours; group 3 after 6 hours and 72 hours; group 4 after 96 hours; group 5 after 120 hours; and group 6 after 144 hours. Plasma samples were extracted, and decaBDE and its metabolites were quantified. Based on comparison to plasma levels (area under the curve [AUC]) following i.v. injections, the oral bioavailability (the percent of the dose reaching systemic circulation) was calculated to be 26% in the rat. The mean maximum plasma concentration (C_{max}) following oral dosing was 264 pmol/mL in the 6-hour sample.

One of the limitations of the absorption data for decaBDE is a lack of knowledge about the mechanism of gastrointestinal absorption. Passive diffusion across the lipid membrane appears to be restricted to lipophilic compounds with low molecular weight rather than high molecular weight compounds such as decaBDE. Accordingly, facilitated transport and/or uptake with dietary lipids by way of the chylomicrons may provide routes for absorption.

In a gavage study by Morck et al. (2003), male Sprague-Dawley rats (n = 8) received 3 μmol/kg (2.9 mg/kg) ^{14}C-labeled decaBDE diluted with unlabeled compound (>98% purity, 15 Ci/mol), prepared by dissolving the decaBDE labeled/unlabeled mixture in toluene, followed by sonication, suspension in Lutrol F127/soy phospholipone/water vehicle, and evaporation of the toluene by nitrogen flow. Four rats were sacrificed after 3 days and the other four rats after 7 days. Urine and feces were collected at 24-hour intervals for 3 and 7 days, respectively, and assayed for radioactivity. Two additional male Sprague-Dawley rats were bile-duct-cannulated, treated similarly with ^{14}C-labeled decaBDE, and sacrificed 3 days later. Bile from these rats was collected and assayed for radioactivity.

Results indicated that in the conventional rats, about 90% of the dose was excreted in the feces within 3 days after a single oral dose of ^{14}C-labeled decaBDE, and the majority of this radioactivity (65%) represented decaBDE metabolites. Radioactivity in bile collected from the cannulated rats accounted for 10% of the fecal excretion. Almost all of the excreted radioactivity in the bile represented metabolites, indicating that at least 10% of the decaBDE dose had been absorbed. It is also possible that greater than 10% of the oral dose may have been absorbed since 65% of the radioactivity excreted in the feces was in the form of metabolites. However, interpretation of the data is difficult. The relatively large amount of metabolites excreted in the feces could be due to a combination of biliary excretion of metabolites, metabolism of decaBDE by the microflora in the gastrointestinal tract, metabolism in the intestinal epithelium, and/or nonbiliary systemic secretion into the gut.

Hughes et al. (2001) conducted a study to evaluate the in vitro dermal absorption of decaBDE in mice. In this study, the dorsal skin of female hairless (Crl:SKH1-hr–BR) mice was removed, cut to a thickness of 255 μm, and exposed in a flow-through diffusion cell system to carrier-free ^{14}C-decaBDE (>98% purity; specific activity not provided) at doses of 6, 30, or

60 nmol. The percent dose absorbed as measured by the amount of material in the collecting chamber was determined at 6, 12, 18, and 24 hours. Very little compound passed through the skin sections; the percentages of dose reaching the receptor fluid in the collecting chamber after 24 hours ranged from 0.07–0.34% and were inversely related to dose.

For all three doses used in the experiment, the largest portion of the dose was taken up during the first 6 hours: 0.17%, 0.04%, and 0.03% of the applied 6, 30, and 60 nmol decaBDE doses, respectively. Results also showed that the 24-hour cumulative percent of the dose absorbed decreased with increasing applied dose, whereas the mass of chemical absorbed increased with increasing applied dose. This result suggests saturation of uptake at the higher doses. The authors calculated the total for the dose retained in the skin sections and transported to the receptor fluid as 20.5%, 3.3%, and 1.9% of the applied dose for 6, 30, and 60 nmol decaBDE, respectively. Most of the compound taken up in the 24-hour period was retained in the skin. The authors acknowledged that the in vitro results observed in this study using mouse skin may overestimate the amount of decaBDE that would be absorbed by human skin, given that the mouse skin is more permeable to several chemicals, at least in vitro, than rat, pig, or human skin.

3.2. DISTRIBUTION

BDE-209 has very low water solubility and a relatively high K_{ow}. Accordingly, high distribution to adipose tissue might be expected. However, as indicated by the data that follow, that is not the case. Systemic distribution of hydrophilic metabolites, as well as molecular mass and favored conformation, may play a role in the limited uptake by adipocytes. The low uptake of decaBDE into tissue lipids makes it different from the less highly substituted, lower molecular weight polybrominated diphenyl ethers (PBDEs).

3.2.1. Studies in Humans

The human data described below come from monitoring of PBDEs in human populations rather than from measured dosing studies. The data demonstrate that humans are exposed to PBDEs and that absorption and distribution to some tissues occur. The data do not provide information on the quantitative aspects of absorption or the kinetics of tissue retention. Limited data are available on the occurrence of BDE-209 in human biological media. Data, described below, are available for human milk and blood samples and indicate a tendency for BDE-209 to distribute to these tissues. However, thorough distribution studies have not been conducted in humans, and therefore it is not known whether BDE-209 distributes to other tissues as well. The number of samples examined in various studies and countries is small, and therefore the data should not be construed as representative at the national level.

3.2.1.1 *Data in Human Milk*

In a study conducted in 2002 of levels of PBDEs in human milk in the U.S., 47 samples from Caucasian, African-American, and Hispanic nursing mothers 20–41 years of age and living in Texas were analyzed for 13 PBDE congeners (Schecter et al., 2003). Mean and median total concentrations of tribromodiphenyl ether (triBDE) through decaBDE were 74 and 34 ng/g lipid weight (lw). DecaBDE was present in these samples, with a mean concentration of 0.9 ng/g lw (1.2% of total PBDEs in the milk; median concentration not available), suggesting that some decaBDE is absorbed, distributed to mammary tissue, and secreted in human milk during lactation.

Milk samples were collected in 2003 from 40 first-time mothers with 8-week-old infants and residing in urban areas in the Pacific Northwest of the U.S. (Montana, Oregon, and Washington State) and British Columbia, Canada (She et al., 2007). Mean and median total concentrations of 12 tri- through decaBDE congeners were 96 and 50 ng/g lw, respectively. These values are substantially higher than the values reported in the study of Schecter et al. (2003) and could be due to the fact that the mothers in the later study had been nursing for longer periods of time. BDE-47 was found at the highest level, followed by hexabromodiphenyl ether (hexaBDE)-153 and pentabromodiphenyl ether (pentaBDE)-99 and -100. DecaBDE-209 with mean and median concentrations of 0.8 and 0.4 ng/g lw, respectively, was a minor congener in breast milk.

3.2.1.2. *Data in Human Blood*

Sjodin et al. (2001a) reported a finding of BDE-209 in serum samples collected from 12 U.S. blood donors in 1988. The median concentration was <1 pmol/g lw with a range of <1–35 pmol/g lw (approximately <1–35 ng/g lw). These concentrations of BDE-209 were comparable to blood levels collected 10 years later, in 1997, from non-occupationally exposed Swedish female cleaners (Sjodin et al., 1999). There is no demographic or questionnaire information on the donor; therefore, no information is available for assessing exposure sources.

Concentrations of tetrabromodiphenyl ether (tetraBDE) and penta-, hexa-, and decaBDE congeners were measured in serum samples collected during 2004 from a family residing in Berkeley, California (35- and 36-year-old father and mother, respectively, 5-year-old daughter, and 18-month-old son) (Fischer et al., 2006). The 18-month-old was exclusively breast-fed for 6 months and was breast-feeding during the study period. PBDE levels for the sum of the five lower brominated congeners BDE-47, -99, -100, -153, and -154 were much higher in the infant (418 ng/g lw) and child (247 ng/g lw) than in their parents (mother 106 ng/g lw, father 64 ng/g lw). BDE-47 was the predominant congener for all ages, followed by hexaBDE-153, pentaBDE-100, pentaBDE-99, and hexaBDE-154. Levels of BDE-209 in the infant (233 ng/g lw) and child (143 ng/g lw) were unusually high compared with those in the parents (mother

14 ng/g lw, father 23 ng/g lw). The authors suspected house dust and breast milk to contribute appreciably to the child and infant exposures; however, no firm conclusions can be drawn from this study, given the small number of subjects investigated.

Sjodin et al. (1999) investigated the exposure to PBDEs of Swedish workers by comparing blood PBDE concentrations collected in 1997 from personnel at an electronics dismantling plant, clerks working full time in front of computer screens, and a control group of hospital cleaning workers. Electronics dismantling involved grinding plastic goods in a shredder. This process releases airborne particulate matter from plastic parts containing brominated flame retardants. The investigators found decaBDE in the serum of individuals from all three groups (19–20 male and female subjects per group). The median BDE-209 concentration in hospital cleaners was <0.7 pmol/g lw (<9.7 ng/g), with a range of ≤0.3–3.9 pmol/g lw (≤0.3–3.7 ng/g), while the median BDE-209 concentration in computer clerks was <0.7 pmol/g lw (<0.7 ng/g), with a range of ≤0.3–8.0 pmol/g lw (≤0.3–7.8 ng/g). Plasma levels of BDE-209 were significantly higher in the electronics dismantling workers than in the other two groups with a median BDE-209 concentration of 5.0 pmol/g lw (4.8 ng/g, range <0.3–9.9 pmol/g lw [<0.3–9.5 ng/g]). The higher BDE-209 concentration in the serum of the electronics dismantling workers was attributed to the relatively high total BDE-209 concentration in the air of the dismantling hall (mean 36 ng/m^3) and at the shredder (175 ng/m^3) (Sjodin et al., 2001b). The presence of BDE-209 in the blood samples from these three groups of workers qualitatively indicated the bioavailability of BDE-209 in humans, even though this compound is not expected to be greatly bioavailable based on its high molecular mass. There was no correlation between plasma levels of BDE-209 with age or fish consumption (the only food evaluated in the study). The serum concentrations of all PBDE congeners decreased in electronic-dismantling workers after vacation. The median decreases, standardized to 30 days of leave, were 14% for BDE-47, -153, and -154, 30% for BDE-183, and 66% for BDE-209. These results indicate shorter half-lives of the more highly brominated diphenyl ethers. However, serum half-lives were not estimated by the authors.

In another Swedish study, increased BDE-209 in the serum was also found in computer technicians who repair or partially dismantle computers (Jakobsson et al., 2002). The median BDE-209 concentration in groups of 19–20 subjects was 1.6 pmol/g lw (1.5 ng/g) in computer technicians, while it was <0.7 pmol/g lw (<0.7 ng/g) in hospital cleaners and computer clerks. A possible source of exposure is airborne dust particulate matter to which PBDEs strongly adsorb (Sjodin et al., 1999).

Thuresson et al. (2005) assessed the exposure to PBDEs in Swedish workers engaged in manufacturing decaBDE flame-retarded rubber goods or electric cables. A referent group, abattoir (slaughterhouse) workers with no occupational exposure to PBDEs, was also investigated. The commercial decaBDE used was Saytex 102E, consisting mainly of BDE-209 with traces of nonaBDEs (BDE-206, -207, and -208) and unknown octaBDE congeners. Consumption of fatty fish was low in all three groups (median 0.5 meals/month), age ranged between 24 and 60 years, with a median of 40 years in all three groups, and each group consisted of approximately 20 subjects. The concentration of 12 PBDE congeners, ranging from tetra- to decaBDE, was measured in the serum samples of all individuals participating in the study. Elevated serum concentrations of octa-, nona-, and decaBDE were present in serum of workers handling decaBDE flame-retarded rubber. Serum concentrations of BDE-209 were up to 50- to 100-fold higher than those of the referent group. In contrast, the serum concentrations of tetra- to heptaBDEs were similar among rubber workers and referents.

3.2.2. Studies in Animals

No studies were identified regarding distribution of decaBDE in animals after inhalation exposure. Several rodent oral dosing studies were identified and are described below. Sandholm et al. (2003) evaluated the distribution of unlabeled decaBDE in male Sprague-Dawley rats. A group of rats (n = 18) was dosed by gavage with unlabeled decaBDE (>98% purity) in dimethylamide/polyethylene glycol 400/water vehicle at 2 μmol/kg (1.9 mg/kg). Another group of rats (n = 18) was dosed intravenously with the same dose of decaBDE. At specific time intervals, blood samples from three rats per group were collected for up to 144 hours. Plasma samples were extracted, and decaBDE and its metabolites were quantified. Oral results indicated that the mean plasma C_{max} was 264 pmol/mL (253 ng/g) at 6 hours after dosing and AUC was 12 nmol × hour/mL (11.5 μg × hour/mL). The results from the i.v. study indicated that the clearance was 0.60 mg/minute-kg and the apparent volume of distribution at steady state was 1.4 L/kg. Concentrations in other tissues were not measured; therefore, relative tissue distribution could not be determined. However, the identification of decaBDE in the plasma supports other studies, suggesting wide tissue distribution.

Morck et al. (2003) evaluated the distribution of decaBDE (>98% purity) in male Sprague-Dawley rats after oral administration. Four rats were sacrificed 3 or 7 days after administration of 3 μmol/kg (2.9 mg/kg) of ^{14}C-labeled and unlabeled decaBDE combined (15 Ci/mol). Liver, adipose tissue, lung, kidney, adrenal glands, skin, muscle, spleen, testis, thymus, heart, plasma, colon wall and contents, and small intestine wall and contents were collected. Radioactivity was determined in all tissues. Analysis of tissues and organs for radioactivity indicated that approximately 9% of the dose remained in the body at 3 and 7 days. On a fresh weight (fw) adjusted basis, the concentrations at 3 and 7 days were highest in the adrenal glands (1.25 and 0.41 nmol/g fw [1.2 and 0.4 μg/g]), liver (0.55 and 0.20 nmol/g fw [0.7 and 0.2 μg/g]), kidney (0.17 and 0.07 nmol/g fw [0.16 and 0.07 μg/g]), and heart (0.14 and 0.05 nmol/g fw [0.13 and 0.05 μg/g]), respectively. On an lw basis, the plasma and liver had the highest concentrations of radiolabel (22 and 14.9 nmol/g lw [21 and 14 μg/g] on day 3 and

8.8 and 5.3 nmol/g lw [8.4 and 5.1 µg/g] on day 7, respectively), whereas adipose tissue, testis, thymus, spleen, small intestine wall, skin muscle, lung, kidney, adrenal, and heart had low concentrations. These results indicate that decaBDE was not readily distributed to lipid-rich tissues but rather was found in plasma and blood-rich tissues, including liver, kidney, heart, and intestinal wall.

Huwe and Smith (2007) conducted a repeat dosing study of BDE-209 during which a group of 18 male Sprague-Dawley rats were given 0.36 µg/day BDE-209 in an oil-based supplement added to their diets for 21 days. Eight control animals received the same diet and oil-based supplement. At the end of dosing, groups of three animals were sacrificed on days 0, 3, 7, 10, 14, and 21 of a follow-up period that began 24 hours after the last feeding of the treated diet. There was no collection of excreta during the feeding period. Twenty-four hours after the last feeding, the levels of BDE-209 in liver, plasma, gastrointestinal tract, and carcass were measured. The highest levels were found in the liver (48.2 ± 8.9 µg/g wet weight) and gastrointestinal tract (35.9 ± 8.5 µg/g wet weight). The amounts in plasma (3.6 ± 0.9 µg/g wet weight) and carcass (14.0 ± 4.0 µg/g wet weight) were lower. After the 21-day exposure, the tissues of the exposed rats contained levels of BDE-209 that were 10–20 times greater than those in control rats. In addition, hepta-, octa-, and nonaBDEs were isolated in tissues and were apparently formed via reductive debromination of BDE-209. Two of the octaBDE congeners (BDE-201 and -197) bioconcentrated in the tissues to a greater extent than the parent and other debrominated metabolites. Huwe and Smith (2007) made no attempt to determine if hydroxylated metabolites had been formed. These results differ from those for the tetra-, penta-, and hexaBDE congeners, where there is no evidence for debromination in the absence of hydroxylation.

Viberg et al. (2003a) studied the distribution of decaBDE in mice. NMRI male mice (n = 6–8) received a single oral dose (2.22 mg/kg) of ^{14}C-decaBDE (40.5 µCi/kg) by gavage on postnatal day (PND) 3, 10, or 19. The animals were sacrificed 1 and 7 days after administration of the radiolabeled decaBDE, and the label in the brain, heart, and liver was measured. The highest concentrations as a percentage of the administered dose were seen in the liver, followed by the brain and heart. The authors did not state whether the radioactivity was that of the parent compound or its metabolites.

One day after administration, the mean radioactivity in the liver of mice treated with radiolabeled decaBDE on PND 3, 10, or 19 was 12.6%, 9.4%, or 5.8% of the administered dose, respectively, whereas 7 days after administration, the radioactivity decreased significantly to 4.8%, 4.6%, or 0.3%, respectively. The distribution to and retention by the liver was greater for the dosing on PNDs 3 and 10 than for the dosing on PND 19. One day after administration, mice treated on PNDs 3 and 10 had 0.5 and 0.4% of total activity administered, respectively, in the brain, and the radioactivity increased to 0.7 and 1.1%, respectively, 7 days after the dosing. In contrast, mice treated with ^{14}C-decaBDE on PND 19 had only 0.06% of the total radioactivity administered in the brain 1 and 7 days after administration. Significant age-dependent differences in distribution to the liver and developing brain were noted. On the other hand, the amount of radioactivity in the heart was minimally affected by age of the animal 24 hours after administration (0.28, 0.31, and 0.22% of the total dose was measured in the heart 24 hours after administration on PNDs 3, 10, and 19, respectively). After 7 days of administration, the 3-day-old and 10-day-old animals did not have significant changes in the amounts of radioactivity in the heart (0.34 and 0.32% of the total administered dose). The amount of radioactivity detected in the hearts of 19-day-old mice had decreased significantly to 0.08%.

In a study by el Dareer et al. (1987) the liver of rats fed two diets containing low (0.0277%; 25 mg/kg) or high (4.8%; 4,400 mg/kg) amounts of ^{14}C-labeled decaBDE contained 0.45, 0.21, and 0.11% of the administered dose on days 1, 2, and 3 after administration of the low dose and 0.007, 0.007, and 0.016% after administration of the high dose, respectively. These data are also included in Appendix O of the National Toxicology Program (NTP) (1986) report. These results suggest saturation in uptake or distribution. High-pressure liquid chromatography and ultraviolet spectral analysis indicated that 81% of the radioactivity in the liver was decaBDE rather than metabolites. The maximum percent of dose in the organs and tissues obtained from the rats fed the lower dose of decaBDE (0.0277%) was in the following order: liver > skin > muscle > fat > blood > gut tissue > plasma > kidneys > lungs > spleen > brain.

Hakk et al. (2002) investigated the disposition of decaBDE in rats. Groups of four male Sprague-Dawley rats (conventional rats) and bile-duct-cannulated rats (cannulated rats) were administered ^{14}C-labeled decaBDE (>97% purity; 15 mCi/mol) in Lutrol F127/soya phospholipid/water vehicle as a single oral dose of 3 µmol/kg (2.9 mg/kg). Gastrointestinal mucosa, kidneys, liver, and lungs were collected from the animals 72 hours following dosing. Radioactivity content was assayed in tissue supernatants and protein-bound extracts. Radioactivity was also quantified from pellets obtained after centrifugation of homogenized tissues. In addition, binding of radiolabeled decaBDE and/or its metabolites to liver proteins was determined. Analysis of liver, lung, intestinal cells, and kidney tissues of noncannulated rats 72 hours following decaBDE administration indicated that the majority (>45–80%) of the decaBDE-derived radioactivity was associated with the membrane fraction, whereas 0–29% and 4–24% were associated with microsomal and soluble fractions, respectively.

Collectively, these studies suggest wide tissue distribution, although relative distribution among various tissues differed across studies in adult rodents. Significant age-dependent differences in distribution to the undeveloped brain were noted.

3.3. METABOLISM

Oral and i.v. studies suggest that decaBDE is metabolized through oxidative dehalogenation reactions to form phenolic metabolites and debrominated to form a variety of nona-, octa-, and heptaBDE congeners. This conclusion is based on the extensive presence of metabolites in the fecal matter and in blood. However, the sites of metabolism have not been identified. At least a portion is likely to occur in the liver. Extrahepatic metabolism may occur in the epithelium of the gastrointestinal tract or through preabsorption metabolism of decaBDE by the intestinal microflora. Figure 3-1 provides a summary of the proposed metabolic pathway as derived from the metabolites that have been identified in plasma, tissues, and fecal material.

It should be noted that some metabolites may be formed by intestinal microbes. The number of bromines removed will depend on whether the starting material is the parent or a partially debrominated metabolite. If absorption occurs with lipids via the chylomicrons, other tissues may also participate in metabolism. The identification of the feces as the major excretory pathway and the high percentage of metabolites present in the feces that cannot be accounted for through biliary excretion provide support for the hypothesis that the liver may not be the only site for metabolic conversions.

Morck et al. (2003) studied decaBDE metabolism in rats given a single oral dose by gavage. Results indicated that in noncannulated rats about 90% of the dose was excreted in the feces within 3 days after a single oral dose of ^{14}C-labeled decaBDE and the majority of this radioactivity (65%) represented decaBDE metabolites. Measurement of bile radioactivity indicated that close to 10% of the total dose was excreted in the bile during the same period, with almost all of the excreted dose in bile in the form of metabolites.

Analysis of radiolabeled materials from tissues of these rats at day 3 after decaBDE administration revealed that 42% of the radioactivity in the liver represented solvent extractable lipid-bound metabolites and 30% was in the form of extractable unconjugated metabolites (4 and 26% of which were hydroxylated and neutral metabolites, respectively). Twenty-seven percent of the radiolabel could not be extracted and was tissue bound. Only 1% of the extractable material was water soluble. A larger percentage (61%) of the radioactivity in the small intestine wall was tissue bound. Lipid-bound metabolites accounted for 7% of the label, water-soluble compounds for 11%, and unbound parent or metabolites for 20%. The percentage of the radiolabel found as water-soluble compounds in the intestinal wall was 10 times greater than the water-soluble metabolites in the liver, providing some support for the hypothesis that oxidative metabolism can occur in the intestinal mucosa. Most of the radioactivity (71–80%) in the lung, adipose tissue, and kidney was unbound parent or metabolites; 15–21% represented lipid-bound metabolites, and 1.5–8% was tissue bound. Formation of adducts was indicative of covalent and/or noncovalent interactions with cellular macromolecules.

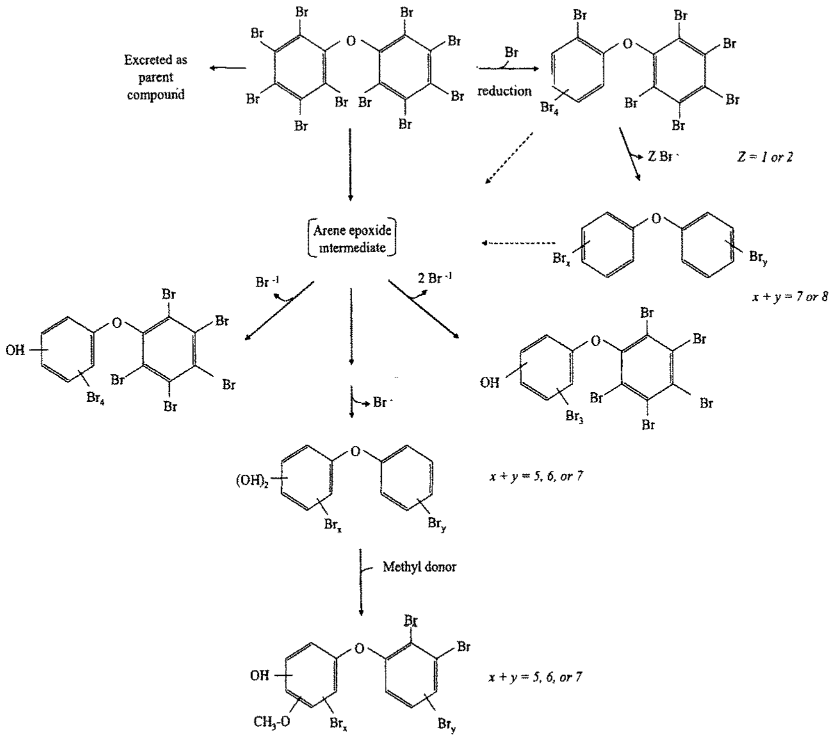


Figure 3-1. Proposed metabolic pathway for BDE-209.

Source: Derived from Huwe and Smith (2007), Sandholm et al. (2003), and Morck et al. (2003).

Sandholm et al. (2003) evaluated the metabolism of unlabeled decaBDE in male rats after gavage or i.v. injection. Blood samples were collected at specific intervals for up to 6 days. Pooled plasma samples from all 6 days were extracted and decaBDE and its metabolites were quantified. Analysis of the pooled samples indicated that the major neutral compound in the plasma was unmodified decaBDE with trace amounts of three nonaBDEs. Thirteen phenolic metabolites were determined in the plasma of both the orally and i.v. dosed rats, but only three phenolic metabolites were present in sufficiently high concentration for further analysis. These metabolites were characterized as a hydroxy-octaBDE, an hydroxy-nonaBDE, and an hydroxy/methoxy hexaBDE (Figure 3-1). The relative amount of each metabolite recovered was not reported, but the concentration of phenolic radioactivity in the plasma collected 3 and 7 days after oral gavage was four times higher than that of the neutral compounds (i.e., the parent or debrominated decaBDE). The authors indicated that reductive debromination may be the first step in the metabolic pathway of decaBDE, followed by oxidation to form phenolic metabolites. It was also suggested that the hydroxy/methoxy metabolites were probably formed via an arene oxide hydrolyzed to a dihydrodiol and further rearomatized followed by a methylation reaction (Figure 3-1).

In the study conducted by Morck et al. (2003), the unconjugated phenolic fractions isolated from the feces were examined by gas chromatography/mass spectrometry (GC/MS). Methoxyhydroxylated penta- to heptabrominated diphenyl ethers were identified. As was the case in the Sandholm et al. (2003) study, the methoxy and hydroxy substituents were on the same phenyl ring when both were present. In addition, trace amounts of debrominated metabolites and nonaBDEs were also found in the feces and bile (see Figure 3-1), indicating debromination may have been the first step in decaBDE metabolism. A small proportion of monohydroxylated metabolites was found in tissues and feces, indicating a role for reductive dehalogenation followed by an oxidation step or direct oxidative dehalogenation reactions.

The plasma samples collected during the Morck et al. (2003) study were analyzed and reported by Sandholm et al. (2003). As was the case with the plasma samples collected by Sandholm et al. (2003), the neutral fraction was almost all BDE-209 with a small fraction of three nonaBDEs. Neutral compounds represented 19% of the plasma total in the samples drawn at 3 days and 21% in the samples collected at 7 days. The phenolic compounds in the plasma could not be purified enough to allow GC/MS analysis.

Huwe and Smith (2007) identified nonhydroxylated metabolites found in feces and tissues after 21 days dosing with 0.36 µg/day BDE-209 in an oil-based supplement added to their diets. Only 5% of the parent dose was present in the body after 21 days of dosing. Three nonaBDEs (206, 207, and 208), four octaBDEs (196, 197, 201, and 203), and one heptaBDE (183) were identified in the body tissues. No attempt was made to determine if hydroxylated metabolites were present. The results are indicative of considerable fecal excretion during the dosing period.

Intravenous administration of 1.07 mg/kg decaBDE to rats (el Dareer et al., 1987; NTP, 1986) resulted in the major part of the dose (74%) being excreted as metabolites in feces. About 63% of the excreted material in the feces was metabolites, and the remaining 37% was unchanged decaBDE. In these rats, 1% of the radioactivity in the bile was intact decaBDE, while 99% of the radioactivity excreted in the bile was in the form of metabolites.

Animal studies indicated that decaBDE is a weak inducer of the phase I or phase II xenobiotic metabolizing enzymes responsible for oxidation and conjugation of many xenobiotic compounds (Darnerud et al., 2001). Zhou et al. (2001) conducted a study in weanling rats to investigate the mechanism(s) by which decaBDE interferes with thyroid hormone homeostasis. In this study, Long-Evans female rats (eight animals/dose group) were orally administered decaBDE (>98% purity) in corn oil at doses of 0, 0.3, 1, 3, 10, 30, 60, or 100 mg/kg-day for 4 consecutive days. Hepatic enzyme activities (ethoxyresorufin O-deethylase [EROD], a marker for cytochrome P-450 1A1 [CYP-1A1]; pentoxyresorufin O-deethylase [PROD], a marker for CYP-2B1) were measured. PROD activity increased only at 1 and 30 mg/kg-day. The lack of dose dependence was also found for EROD activity, where maximal induction was only 1.8-fold in the 1 mg/kg-day group, indicating that there were no significant or dose-related effects on CYP-1A1 or CYP-2B1. However, the presence of active EROD and PROD suggests that there may be some oxidative debromination of the decaBDE during metabolism, through the activity of CYP-1A1 and/or CYP-2B1.

Pacyniak et al. (2007) evaluated the ability of BDE-209 to induce CYP-3A11, -2B10, and -1A1/2. Six C57BL/mice (10 weeks of age) were injected with doses of 10 or 100 μmol/kg (10 or 100 mg/kg) in corn oil for 4 days. The livers were removed 24 hours after the last dose and the levels of messenger ribonucleic acid (mRNA) measured by Northern blot and branched deoxyribonucleic acid (bDNA) analyses. The bDNA was considered to be the more accurate of the two assay systems. Northern blot analysis indicated that the levels of CYP-2B10 were induced three- and fivefold, respectively, at the two doses tested, while the bDNA results indicated 3.6-fold and sevenfold inductions. CYP-3A11 did not show a difference with respect to the dose administered but was induced 4-fold by the Northern blot analysis and 1.7-fold by the bDNA analysis. The two doses of PBDE-209 induced CYP 1A1/2 9- and 6-fold, respectively, by Northern blot analysis and 0.3- and 0.8-fold by bDNA analysis.

3.4. ELIMINATION

As has been mentioned previously, the excretion of decaBDE and its metabolites in rats is almost exclusively through the fecal and biliary routes. In toxicokinetic studies (Morck et al., 2003; Hakk et al., 2002; el Dareer et al., 1987), the amounts excreted in urine have consistently been less than 1% of the dose (about 18% bound to albumin); biliary excretion has accounted for about 10% of the label found in the feces. There have been no studies that examined the excretion of BDE-209 in mice. Studies by Staskal et al. (2006) using BDE-47, -99, and -153 found that urinary excretion in male mice involves binding with one or two major urinary excretory proteins.

In one of the early toxicokinetic studies (el Dareer et al., 1987; NTP, 1986), the fate of decaBDE in male F344 rats was investigated. The study consisted of four substudies. In substudy one, groups of 2-month-old male F344 rats (three animals/group) were fed a standard diet containing unlabeled decaBDE (92% purity) on days 1–7 and 9–11 and the test diet containing ^{14}C-labeled decaBDE (>98% purity) on day 8. The diets contained 0, 0.0250, 0.0509, 0.250, 0.487, 2.49, or 4.99% decaBDE. Based on the rat body weight information reported in el Dareer et al. (1987) and the average feed intake from the NTP (1986) report, the corresponding daily doses were 0, 27, 55, 272, 512, 2396, or 4577 mg/kg. Radioactivity was determined in feces collected daily on study days 9–12.

In substudy two, rats were fed two diets containing low (0.0277% or 25 mg/kg) or high (4.80% or 4400 mg/kg) amounts of decaBDE or similar amounts of ^{14}C-labeled decaBDE, using the same protocol as in the first substudy, except that groups of three rats were killed on study days 10, 11, or 12. Urine and feces were collected from each rat and analyzed for radioactivity.

In substudy three, a group of rats (n = 3) was injected intravenously via the tail vein with 1.07 mg/kg of ^{14}C-labeled decaBDE; urine and feces were collected daily for 3 days and analyzed for radioactivity 72 hours after dosing. In the fourth substudy, bile-duct-cannulated rats (n = 5) were injected intravenously with 0.947 mg/kg of ^{14}C-labeled decaBDE. Bile was collected over a 4-hour period. Radioactivity was determined in each pooled bile sample.

The recovery of radioactivity in the feces ranged from 91–101% of the ingested dose in the first feeding study and 83–86% in the second feeding study, indicating that the recovery was not related to the dose of decaBDE or to the time of sacrifice (24, 48, or 72 hours) after consumption of ^{14}C-labeled decaBDE within a specific substudy. (Note: no reasons were given for the differences in the radioactivity recovered in these two studies.) Greater than 99% of the radioactivity was recovered in the feces and gut contents.

After i.v. dosing of ^{14}C-labeled decaBDE (substudy three), 74% of the radioactivity was recovered in the feces and gut contents at 72 hours. About 63% of the excreted material in the feces was metabolites and the remaining 37% was unchanged decaBDE. In these rats, only traces of radioactivity were noted in the urine. In bile-duct-cannulated rats, 7.2% of the radioactivity intravenously administered appeared in the bile in 4 hours, 1% of which was intact decaBDE (i.e., 99% of the radioactivity excreted in the bile was in the form of metabolites). Together, these results show that the vast majority of an oral dose of decaBDE is excreted in the feces, mostly as unabsorbed material.

Morck et al. (2003) administered orally ^{14}C-radiolabeled decaBDE as a single 3 μmol/kg (2.9 mg/kg) dose in soy phospholipid/Lutrol F127/water vehicle to male Sprague-Dawley rats (i.e., conventional rats). An average of 90 and 91% of the radioactivity was excreted in the feces at 3 and 7 days, respectively. About 71% of the total dose was excreted in the first 24 hours, another 17% between 24 and 48 hours, and a further 2% between 48 and 72 hours. In bile-duct-cannulated rats subjected to the same oral treatment, an average of 88% of the dose was excreted in the feces and 9.5% in the bile within 3 days. Less than 0.1% of the radioactivity was excreted in the urine. In the cannulated rats, 66% of the total dose was excreted in the feces in the first 24 hours and another 19% during 24–48 hours. In the first 12 hours, 4.4% of the total dose was recovered in the bile, whereas 1.6, 2, and 0.4% of the total dose were excreted at 12–24, 24–48, and 48–72 hour intervals, respectively. These results indicate that excretion of decaBDE via feces was the dominant route after the oral dose, and biliary excretion plays a major role in the systemic elimination of absorbed decaBDE. The urinary excretion of radioactivity was insignificant.

In the Hakk et al. (2002) study described earlier, ≤0.02% of the administered decaBDE dose was excreted daily via the urine in both conventional and cannulated rats, with a total of 0.033 and 0.047%, respectively, of the administered dose excreted over the 72-hour period. About 9% of the administered dose was excreted in the bile by 72 hours, 6% of which was eliminated within the first 24 hours, indicating that excretion via the bile was favored over that of urine.

About 20% of the decaBDE-derived radioactivity in urine from noncannulated rats was protein bound at 72 hours (compared to >73% not associated with protein). Eighteen percent of the bound material was bound to albumin, a serum protein with the ability to bind (nonspecific protein binding) short chain fatty acids. In cannulated rats, 18.2% of the decaBDE-derived radioactivity was unbound, and all the remaining 68.3% was associated with albumin. Two polar metabolites were noted but not identified. Under the assumption that the bound materials are less polar than the unbound materials, this observation supports the concept that a substantial portion, but not all, of the metabolites in the fecal matter originate from the bile.

About 90% of the biliary radiolabel was associated with an unidentified 79-kDa protein, with the percent of bound label decreasing from 94 to 87% in bile samples pooled at 1–24 hours, 24–48 hours, and 48–72 hours. Approximately 17% of the protein-bound biliary radioactivity collected over the first 24 hours was parent compound (and the remainder was unidentified metabolites); no parent compound was detected at 48 and 72 hours. The percent of total bound label in the bile samples also declined over time. None of the label in the bile was found to be unbound.

3.4.1. Half-life Estimates

In computer technicians, the half-life of BDE-209 is estimated to be in the range of a week (Sjodin et al., 2003; Jakobsson et al., 2002); however, the data to support this estimate are limited. Sjodin et al. (1999) also found that the levels of BDE-209 in the blood of occupationally exposed Swedish workers decreased by 66% over a 30-day absence from the workplace. These authors did not present any half-life estimate in their publication.

The half-lives of hepta- to decaBDE in human serum were estimated by using data from occupationally exposed workers sampled before, during, and after a vacation period (Thuresson et al., 2006). The half-lives were found to decrease with increasing bromination. The half-life of heptaBDE-183 was 94 days, while that for BDE-209 was 15 days.

Sandholm et al. (2003) evaluated the kinetics of unlabeled decaBDE in male rats. One group of rats was dosed orally by gavage with 2 µmol decaBDE/kg (1.9 mg/kg). Another group of rats was also dosed intravenously with unlabeled decaBDE at the same dose. At specific time intervals, blood samples from three rats per group were collected according to the following schedule: group 1 was sampled 1 hour and 24 hours after dosing, group 2 after 3 hours and 48 hours, group 3 after 6 hours and 72 hours, group 4 after 96 hours, group 5 after 120 hours, and group 6 after 144 hours. Plasma samples were extracted and decaBDE and its metabolites were quantified. Results from animals orally dosed with unlabeled decaBDE indicated the mean C_{max} in plasma reached 264 pmol/mL (253 ng/g) at 6 hours after dosing and AUC was 12 nmol × hour/mL (11.5 µg × hour/mL). The i.v. data indicated that the clearance was 0.60 mg/minute-kg, and the apparent volume of distribution at steady state was 1.4 L/kg.

Half-lives were determined from the slope of the total concentration-time curve by linear regression. The disposition of decaBDE in male rats after oral dosing was described by a two-compartment model with $t_{1/2\beta}$ and $t_{1/2\gamma}$ values of 6.9 hours and 51 hours, respectively. The results from the i.v. study were consistent with a three-compartment model with half-lives ($t_{1/2\alpha}$, $t_{1/2\beta}$, and $t_{1/2\gamma}$) of 1.6 hours, 12 hours, and 58 hours, respectively (Sandholm et al., 2003). This value is lower than the 15-day half-life for humans estimated by Thuresson et al. (2006).

Huwe and Smith (2007) modeled the distribution and elimination half-lives of parent BDE-209 and several debrominated nonhydroxylated metabolites based on assays of plasma, excreta, liver, and carcass over a 21-day period that followed 21 days of dosing with 0.36 µg/day. The BDE-209 data showed the best fit to a biphasic depletion pattern. The distribution half-lives were 1.0 and 1.2 days for liver and plasma, respectively. The elimination half-lives for the same tissues were 20.2 and 75.9 days, respectively. A plasma first order half-life for octaBDE-207 (7.9 days) was twice that of BDE-209 (3.9 days). In the liver, the first order half-life estimates for congeners 208, 191, and 197 (~6 days) were greater than those for 206 and 207 (~1 day). First-order estimates for 207 and 196 were intermediate (4–5 days). These values reflect the behavior of the parent BDE-209 and the debrominated, nonhydroxylated metabolites after absorption, distribution, and excretion but do not reflect the distribution and elimination of the hydroxylated metabolites.

3.5. PHYSIOLOGICALLY BASED TOXICOKINETIC MODELS

Limited information is available on the absorption, distribution, metabolism, and excretion of decaBDE in experimental animals and in humans. A model for human metabolism has not been established. Extrapolation of results from laboratory animals to humans using physiologically based pharmacokinetic (PBPK) models is not possible at this time.

4. HAZARD IDENTIFICATION

4.1. STUDIES IN HUMANS—EPIDEMIOLOGY, CASE REPORTS, CLINICAL TRIALS

Studies of decaBDE levels in occupationally exposed groups or studies of decaBDE in human biological media did not include surveillance of health endpoints.

4.2. SHORT-TERM, SUBCHRONIC, AND CHRONIC STUDIES AND CANCER BIOASSAYS IN ANIMALS—ORAL AND INHALATION

Inhalation toxicological studies of decaBDE in experimental animals are not available.

4.2.1. Short-term and Subchronic Studies

The short-term and subchronic studies are summarized in Table 4-1.

4.2.1.1. *Studies in Rats*

Zhou et al. (2001) conducted a study in weanling rats to investigate the mechanism(s) by which decaBDE interferes with thyroid hormone homeostasis. In this study, Long-Evans female rats (eight animals/dose group) were orally administered decaBDE (>98% purity) in corn oil at doses of 0, 0.3, 1, 3, 10, 30, 60, or 100 mg/kg-day for 4 consecutive days. Body weights were recorded and dosing volumes adjusted daily. Animals were sacrificed 1 day after the last dose. ~~Serum total thyroxine (T_4) and triiodothyronine (T_3), serum thyroid stimulating hormone (TSH),~~ and hepatic enzyme activities (EROD, a marker for CYP-1A1; PROD, a marker for CYP-2B1; and T_4-uridine diphosphate glucuronyl transferase [T_4-UDPGT]) were measured (see section 3.3 for data on EROD and PROD). Short-term treatment with decaBDE did not cause any visible signs of toxicity or any effects on body-weight gain or liver-to-body-weight ratios at any dose level. DecaBDE (up to 100 mg/kg-day) had no effect on serum T_4, T_3, or TSH concentration or on hepatic UDPGT activity. Based on these observations, the highest dose of 100 mg/kg-day is identified as the no-observed-adverse-effect level (NOAEL).

Carlson (1980) conducted a study to evaluate the induction of xenobiotic metabolism in rats, following short-term administration of decaBDE. Groups of four male Sprague-Dawley rats were dosed orally with 0.1 mmol/kg-day (96 mg/kg-day) of decaBDE in corn oil for 14 days. The decaBDE was synthesized by the complete bromination of diphenyl ether and was reported to be of "high purity." These animals were probably dosed every other day since the protocol stated that livers were collected from animals sacrificed 24 hours after the last (seventh) dose.

Table 4-1. Oral short-term and subchronic toxicity studies for decaBDE in laboratory animals

Study	Species, sex, and sample size	Route, dose, and duration	Observed effects	NOAEL	LOAEL[a]	Comments
Zhou et al. (2001)	Rat, Long-Evans, female weanling rats, 8/dose group	Gavage (>98% purity); 0, 0.3, 1, 3, 10, 30, 60, or 100 mg/kg-day; 4 days	No observed dose-related effects on body weight or liver weight or changes in T_3 or T_4 levels	100 mg/kg-day	Not identified	
NTP (1986)	Rat, F344/N, male and female, 5/sex/dose group	Diet (99% purity); 0, 472, 928, 1,846, 4,569, or 9,326 mg/kg-day in males; 0, 538, 1,061, 2,137, 5,323, or 10,853 mg/kg-day in females; 14 days	None	9,326 mg/kg-day in males; 10,853 mg/kg-day in females	Not identified	Survival, final mean body weights not adversely affected. Clinical signs or gross pathological effects not noted.
NTP (1986)	Rat, F344/N, male and female, 10/sex/dose group	Diet (97–99% purity); 0, 191, 372, 781, 1,536, or 3,066 mg/kg-day in males; 0, 238, 504, 967, 1,955, or 3,944 mg/kg-day in females; 13 weeks	None	3,066 mg/kg-day in males; 3,994 mg/kg-day in females	Not identified	Survival, final mean body weights not adversely affected. Clinical signs or gross pathological effects not noted.
NTP (1986)	Mouse, B6C3F1, male and female, 5/sex/dose group	Diet (99% purity); 0, 1,027, 2,143, 4,246, 10,536, or 20,994 mg/kg-day in males; 0, 1,146, 2,286, 4,627, 11,348, or 23,077 mg/kg-day in females; 14 days	None	20,994 mg/kg-day in males; 23,077 mg/kg-day in females	Not identified	Survival, final mean body weights not adversely affected.
NTP (1986)	Mouse, B6C3F1, male and female, 10/sex/dose group	Diet (97–99% purity); 0, 666, 1,355, 2,659, 5,278, or 10,233 mg/kg-day in males; 0, 702, 1,437, 2,899, 5,687, or 11,566 mg/kg-day in females; 13 weeks	None	10,233 mg/kg-day in males; 11,566 mg/kg-day in females	Not identified	Survival, final mean body weights not adversely affected. Clinical signs or gross pathological examination did not show any effect.

[a]LOAEL = lowest-observed-adverse-effect level.

Detoxification of O-ethyl O-p-nitrophenyl phenylphosphonothioate, methylation of p-nitroanisole, levels of NADPH cytochrome c reductase and cytochrome P-450 (CYP-450), and activities of UDPGT and benzo[a]pyrene hydroxylase were determined in hepatic cytosol or microsomes. Serum sorbitol dehydrogenase measurements were also performed on blood samples collected from the tail vein. No significant changes were observed in these enzyme activities. DecaBDE significantly increased the liver-to-body-weight ratio, indicating liver enlargement. Sorbitol dehydrogenase activity in the serum was not altered by decaBDE, suggesting that liver necrosis had not occurred, although other common serum markers for liver damage were not measured. Because of limitations in the study design, these results are not adequate for use in the health assessment of decaBDE.

NTP (1986) conducted a 14-day study in rats exposed to decaBDE. F344/N rats (five animals/sex/dose) were fed diets containing 0, 5,000, 10,000, 20,000, 50,000, or 100,000 ppm decaBDE (99% purity). Based on the reported body weight information NTP (1986) and U.S. EPA (1988) default food intake values for F344 male (0.018 kg food/day) and female (0.014 kg food/day) rats, the corresponding estimated average daily doses were 0, 472, 928, 1,846, 4,569, or 9,326 mg/kg-day in male rats and 0, 538, 1,061, 2,137, 5,323, or 10,853 mg/kg-day in female rats. Animals were observed daily and were weighed on days 1, 7, and 14. At the end of the exposure period, animals were necropsied and several organs and tissues were examined histologically. No mortality was observed in the rats during the course of the study. Exposure to decaBDE did not cause any clinical signs of toxicity or adversely affect the final mean body weights. Gross pathological effects were not noted in any animal at any dose level. The results of this study indicated a NOAEL of 9,326 mg/kg-day in male rats and 10,853 mg/kg-day in female rats.

The subchronic effects of decaBDE (97–99% purity) on rats were also investigated in a 13-week study (NTP, 1986). Groups of F344/N rats (10/sex/dose) were administered decaBDE in the diet at concentrations of 0, 3,100, 6,200, 12,500, 25,000, or 50,000 ppm for 13 weeks. Based on body-weight information in the NTP (1986) report and U.S. EPA (1988) default food intake values for F344 male (0.018 kg food/day) and female (0.014 kg food/day) rats, the corresponding estimated average daily doses were 0, 191, 372, 781, 1,536, or 3,066 mg/kg-day in male rats and 0, 238, 504, 967, 1,955, or 3,944 mg/kg-day in female rats. Animals were observed twice daily and body weight, feed consumption, clinical signs, and behavior were recorded once a week. A necropsy was performed on all animals, including those killed in extremis, with the exception of those excessively autolyzed or cannibalized. Histologic examination was performed on major organs and tissues from control and high-dose groups. No mortality was observed in rats fed decaBDE, and no clinical signs of toxicity were noted. Compound-related changes in body weight and feed consumption were not observed, and no gross or macroscopic pathological effects were noted in any animal examined. The results indicate a NOAEL of 3,066 mg/kg-day in male rats and 3,944 mg/kg-day in female rats.

4.2.1.2. *Studies in Mice*

A 14-day study (NTP, 1986) was also conducted in mice. B6C3F1 mice (five animals/sex/dose) were fed diets containing 0, 5,000, 10,000, 20,000, 50,000, or 100,000 ppm decaBDE (99% purity). Based on the reported body weight information (NTP, 1986) and U.S. EPA (1988) default food intake values for B6C3F1 male (0.0057 kg food/day) and female (0.0048 kg food/day) mice, the estimated average daily doses were 0, 1,027, 2,143, 4,246, 10,536, or 20,994 mg/kg-day in male mice and 0, 1,146, 2,286, 4,627, 11,348, or 23,077 mg/kg-day in female mice. Animals were observed daily and were weighed on days 1, 7, and 14. Necropsy was performed at the end of the exposure period, and several organs and tissues were examined histologically. Exposure to decaBDE up to 20,994 mg/kg-day in males and 23,077 mg/kg-day in females showed no effects on survival or body weight, and there were no clinical signs of toxicity. No compound-related gross pathological effects were noted in any animal in any group. The results of this study indicate a NOAEL of 20,994 mg/kg-day in male mice and 23,077 mg/kg-day in female mice.

B6C3F1 mice (10 animals/sex/dose) were fed diets containing 0, 3,100, 6,300, 12,500, 25,000, or 50,000 ppm decaBDE (97–99% purity) for 13 weeks (NTP, 1986). Based on the mouse body weight information reported (NTP, 1986) and U.S. EPA (1988) default food intake values for B6C3F1 male (0.0057 kg food/day) and female (0.0048 kg food/day) mice, the corresponding estimated average daily doses were 0, 666, 1,355, 2,659, 5,278, or 10,233 mg/kg-day in males and 0, 702, 1,437, 2,899, 5,687, or 11,566 mg/kg-day in females. Animals were observed twice daily and body weights, feed consumption, clinical signs, and behavior were monitored once a week. Necropsy was performed on all animals, including those killed in extremis, with the exception of those excessively autolyzed or cannibalized. Histologic examination was performed on the organs and tissues from control and high-dose groups. Only one male and one female mouse fed 12,500 ppm died in the course of the study. There were no clinical signs of toxicity, and no compound-related effects on body weight and feed consumption were observed. No gross or macroscopic pathological effects were noted in any animal at any dose. The results of this study indicated a NOAEL of 10,233 mg/kg-day in males and 11,566 mg/kg-day in females.

4.2.2. Chronic Studies and Cancer Bioassays

NTP (1986) investigated the relationship between ingestion of decaBDE in rats and mice and tumor development. These chronic oral studies are summarized in Table 4-2. The decaBDE used in both rats and mice was 94–97% pure, with no detectable brominated dioxins or furans.

The major impurities in the decaBDE test material were isolated and identified as two unspecified congeners of nonaBDE.

4.2.2.1. *Study in Rats*

Groups of 7- to 8-week-old male and female F344/N rats (50/sex/dose) were exposed to decaBDE (94–97% purity) in the diet at concentrations of 0, 25,000, or 50,000 ppm for 103 weeks (NTP, 1986). Average daily doses of decaBDE as reported in the study were 0, 1,120, or 2,240 mg/kg-day for male rats and 0, 1,200, or 2,550 mg/kg-day for female rats. The animals were observed twice daily and clinical signs were recorded once per week. Animals were weighed once a week for the first 12 weeks, once per month thereafter until week 100 or 101, then every 2 weeks. Mean body weights were calculated for each group. In addition, feed consumption, morbidity, and mortality were monitored throughout the study period. Animals found moribund and animals that survived to the end of the study period were sacrificed. Complete necropsy was performed on all animals, including those found dead during the course of the study, unless they were excessively autolyzed or cannibalized. Gross and microscopic examinations were performed on major organs or tissues.

No clinical signs of toxicity were observed in the treated rats. There were no significant differences in the mean body weight and feed consumption between treated and control animals. Survival of low-dose male rats was significantly lower than that of the controls after week 102, but the decrease was not considered to be compound related because the reduction in survival occurred late in the study and there was a lack of a dose effect.

At necropsy, several nonneoplastic changes were observed. In the liver, an increase in the incidence of thrombosis was observed in high-dose male rats (1/50, 0/50, 9/49), with no such increase noted in low-dose males or in any female at any dose level. A dose-dependent, but not statistically significant, increase in the incidence of degeneration of the liver was also observed in treated male rats at incidence rates of 13/50, 19/50, and 22/49 in the control, low-dose, and high-dose groups, respectively. No liver degeneration was observed in female rats. In the spleen, an increased incidence of fibrosis was seen in males at low dose (8/50) and high dose (13/49) compared with 5/49 in controls, indicating a dose-dependent increase that was statistically significant only in the high-dose group. Hematopoiesis was observed at an increased incidence in the spleen of female rats (control 12/49, low dose 24/48, high dose 17/50), but the increase was not dose dependent or statistically significant at any dose level. No such increases were observed in males. In the mandibular lymph node, lymphoid hyperplasia increased in males in a dose-dependent manner (4/50, 6/50, and 13/49 in the control, low dose, and high dose, respectively), but the incidence reached statistical significance only at the high dose.

Table 4-2. Oral chronic toxicity studies for decaBDE in laboratory animals

Study	Species, sex, and sample size	Route, dose, and duration	Observed effects	NOAEL	LOAEL[a]	Comments
NTP (1986)	Rat, F344/N, male and female, 50/sex/dose group	Diet (94–97% purity); 0, 1,120, or 2,240 mg/kg-day for males; 0, 1,200, or 2,550 mg/kg-day for females; 2 years	Increased incidences of thrombosis (1/50, 0/50, 9/49) and degeneration (13/50, 19/50, 22/49) in the liver of high-dose male rats; dose-dependent increase in splenic fibrosis in males with statistical significance at high dose; dose-dependent increase in lymphoid hyperplasia of the mandibular lymph nodes in males with statistical significance at high dose Dose-related increase in liver neoplastic nodules statistically significant in low- and high-dose males and in high-dose females	1,120 mg/kg-day in males 2,550 mg/kg-day in females	2,240 mg/kg-day in males Not identified	Males, but not females, exhibited effects.
NTP (1986)	Mouse, B6C3F1, male and female, 50/sex/dose group	Diet (94–97% purity); 0, 3,200, or 6,650 mg/kg-day for males; 0, 3,760, or 7,780 mg/kg-day for females; 2 years	Increased incidences of granulomas in the liver of treated males (with statistical significance only at low dose); centrilobular hypertrophy in males (with significance at low and high doses); dose-dependent increase in thyroid follicular cell hyperplasia (2/50, 10/50, 19/50) in males (significant at low and high doses); increase in the incidence of stomach ulcers in females at high dose Increased incidence of hepatocellular adenoma or carcinoma (combined) in low-dose males; marginally but not statistically significant increase in the thyroid gland follicular cell adenomas or carcinomas (combined) in males	Not available in males 3,760 mg/kg-day in females	3,200 mg/kg-day in males 7,780 mg/kg-day in females	

[a]LOAEL = lowest-observed adverse-effect level.

No incidence of lymphoid hyperplasia was reported in females at any dose level. An increased incidence of retinal degeneration was noted in low-dose female rats but not in high-dose females or males at any dose level. This lesion was attributed to greater exposure of the female rats to fluorescent light and was not considered to be treatment related. Acanthosis (increased thickness of the epithelial surface) of the forestomach was observed at increased incidence in treated males but not in females, but the incidence was not significant. Both male and female rats demonstrated a dose-dependent decrease in the incidence of C-cell hyperplasia in the thyroid gland (12/50, 6/49, and 2/49 in males and 14/50, 7/49, and 2/50 in females at control, low-dose, and high-dose groups, respectively). Decreases in the C-cell hyperplasia would not be considered biologically adverse since other thyroid effects were not observed in these rats. No other significant pathological changes were observed.

Histopathologic examination revealed a significant increase in the incidence of neoplasia in the rat, and several organs or tissues were adversely affected. There was a dose-dependent increase in the incidence of neoplastic nodules in the livers of both male and female rats. The incidence of these lesions was 1/50, 7/50, and 15/49 in males and 1/50, 3/49, and 9/50 in females in control, low-dose, and high-dose groups, respectively. The incidence reached statistical significance at both treatment doses in males and at the high dose in females.

At the time the NTP (1986) study was conducted, the term neoplastic nodule was used to describe abnormal cellular masses in the livers of rats characterized by loss or distortion of normal cellular architecture (Maronpot et al., 1986). Some of those nodules would now be described as benign hepatocellular adenomas in rats (Wolf and Mann, 2005). However, there is no complete equivalency between the neoplastic nodule of the past and the hepatocellular adenoma term of today. Some of the neoplastic nodules from the NTP (1986) study might now be classified as foci of cellular alteration or hyperplasia rather than adenomas (Maronpot et al., 1986). Adenomas and foci of cellular alteration are considered to be preneoplastic lesions, whereas hyperplastic lesions represent secondary nonneoplastic changes (Maronpot et al., 1986). The assumption that the hepatic neoplastic nodules from the NTP (1986) bioassay are equivalent to hepatic adenomas under the current NTP lexicon is a conservative interpretation of the data.

A slight increase in mononuclear cell leukemia in treated rats was observed with incidences in males of 30/50, 33/50, and 35/50 at control, low, and high doses, respectively, and in females of 14/50, 21/50, and 18/50 at control, low, and high doses, respectively. However, the increase was not considered to be biologically significant because of the marginal and insignificant increase in treated rats of both sexes and the high incidence in control rats. The incidence of hepatocellular carcinomas was low in male and female rats and was apparently not compound related. Other tumors observed included splenic sarcomas, pancreatic acinar cell adenomas, carcinomas in Zymbal's gland, and osteosarcomas, but these were considered to be of no significance because of high historical incidence, lack of dose-response trend in the tumor incidence, or lack of statistically significant responses.

Based on the results from this 2-year study in rats (NTP, 1986), exposure to decaBDE in the diet did not cause compound-related effects on survival or any significant effects on body weight or food consumption. However, treatment resulted in several nonneoplastic changes at the high dose, including thrombosis and degeneration of the liver in males, fibrosis in the spleen in males, and lymphoid hyperplasia in the mandibular lymph node in males. Dose-dependent increases in the incidence of neoplastic nodules in liver of males and females provide some evidence of carcinogenicity of decaBDE in rats. Based on these results and on increased incidence of thrombosis and degeneration in the liver, splenic fibrosis, and lymphoid hyperplasia of the mandibular lymph nodes, a NOAEL for systemic toxicity was 1,120 mg/kg-day and the lowest-observed-adverse-effect level (LOAEL) was 2,240 mg/kg-day for males. Female rats appeared to be less sensitive to the systemic toxicity of decaBDE at the doses used in this study. Based on this finding, the NOAEL for systemic toxicity in females was 2,550 mg/kg-day, with no LOAEL established. The dose-related increase in nonmalignant liver tumors (neoplastic nodules) in both males and females provides some evidence of carcinogenicity of decaBDE in rats.

4.2.2.2. *Study in Mice*

Groups of 9-week-old male and female B6C3F1 mice (50/sex/dose) were administered decaBDE (94–97% purity) in the diet at doses of 0, 25,000, or 50,000 ppm for 103 weeks (NTP, 1986). Average daily doses of decaBDE as reported in the study were 0, 3,200, or 6,650 mg/kg-day in male mice and 0, 3,760, or 7,780 mg/kg-day in female mice. The animals were observed twice daily, and clinical signs were recorded once per week. Animals were weighed once a week for the first 12 weeks and once per month thereafter. In addition, feed consumption, morbidity, and mortality were monitored throughout the study period. All survivors were sacrificed during weeks 112–113. Complete necropsy was performed on all animals, including those found dead during the course of the study, unless they were excessively autolyzed or cannibalized. Gross and microscopic examinations were performed on major organs or tissues.

There were no significant differences in survival among any groups of mice of either sex at terminal sacrifice. However, loss of control male mice (presumably due to fighting) was significant during the first 15 months of the study. There were no compound-related clinical signs of toxicity or changes in body weight or food consumption.

At necropsy, several nonneoplastic changes were observed in tissues of treated mice. In the liver, the incidence of granulomas in control, low-, and high-dose mice was 8/50, 22/50, and 12/50 in males and 23/50, 27/50, and 24/50 in females, respectively. Although increases were observed in the treated animals of both sexes compared with controls, no consistent dose response for this effect was evident, and the effect was not associated with a statistically significant positive trend. Thus, the toxicological significance of this effect is unclear. Significant increases in the incidence of centrilobular hypertrophy were also observed in the liver of male mice at high and low doses (0/50, 34/50, and 32/50 in the control, low dose, and high dose, respectively). Although the increases were comparable in the low- and high-dose males and were not observed in female mice at any dose level, the high incidence in the treated males indicates that the effect was treatment related. In the thyroid gland, a dose-dependent and statistically significant increase (at both dose levels) in the incidence of follicular cell hyperplasia was observed in males (2/50, 10/50, and 19/50, respectively, in the control, low-dose, and high-dose groups). In the females, the incidence was increased in the low- (9/50) and high- (7/49) dose groups compared to 4/50 in the control group, but the increase was not dose dependent or statistically significant at any dose level. Only high- but not low-dose female mice exhibited a significant increase in the incidence of stomach ulcers (1/50, 1/50, and 8/50 in the control, low-dose, and high-dose females, respectively). In males, the incidence in treated mice was comparable with that in control mice: 5/49, 3/50, and 5/50 in the control, low-dose, and high-dose males, respectively.

Histopathological examination revealed a significantly increased incidence of neoplasia in mice, with the liver appearing to be the main target organ for decaBDE. In the liver, increases (although not statistically significant) in the incidence of hepatocellular adenoma were observed at similar rates in low- and high-dose males (4/50, 12/50, and 12/50 in control, low-dose, and high-dose groups, respectively). Other changes observed in male mice included an increased incidence of hepatocellular carcinoma (5/50, 14/50, and 8/50 in the control, low-dose, and high-dose groups, respectively) that was not statistically significant at either dose. The combined incidence of hepatocellular adenomas or carcinomas in male mice, after correction for survival, significantly increased at low dose but not at high dose; the responses amounted to 8/50, 22/50, and 18/50 in control, low-dose, and high-dose groups, respectively. As indicated in the study report, these findings may have been influenced by the large number of early deaths in control male mice compared with treated mice, thereby decreasing the significance of the hepatocellular adenomas or carcinomas seen in the treated male mice. Consequently, the apparent statistically significant increase in the hepatocellular adenomas and carcinomas (combined) at the high dose (18/50 versus 8/50) based on regular rate comparison test (i.e., Fisher's exact test) was no longer significant when the life table test or incidental tumor test was used to control for intercurrent mortality. The trend tests from the latter two tests also failed to show statistical significance in the combined hepatocellular adenomas or carcinomas in male rats. The incidence of hepatocellular adenomas or carcinomas (combined) in female mice was not statistically significant (8/50, 13/50, and 13/50 in control, low-, and high-dose mice, respectively). In the thyroid gland, follicular cell adenomas or carcinomas (combined) were slightly, but not significantly, increased in treated mice of both sexes over the corresponding control mice; the incidence was 0/50, 4/50, and 3/50 in males and 1/50, 3/50, and 3/50 in females in the control, low-, and high-dose groups, respectively.

These results from the NTP (1986) chronic carcinogenicity study in mice show that decaBDE treatment caused liver granulomas, liver hypertrophy, and thyroid gland follicular cell hyperplasia in males only and stomach ulcers only in females. Males, but not females, had a statistically significant increase in the incidence of hepatocellular adenomas and carcinomas at the low dose but not at the high dose. Based on these results and on increased incidence of liver granulomas and centrilobular hypertrophy and statistically significant and dose-dependent increases in the thyroid gland follicular cell hyperplasia in male mice administered 3,200 mg/kg-day or higher, no NOAEL for systemic effects for males was established. Female mice were less sensitive to the systemic toxicity of decaBDE at the doses used in this study; however, the IRIS assessment authors identified a NOAEL for a portal-of-entry effect for females of 3,760 mg/kg-day and a LOAEL of 7,780 mg/kg-day based on an increase in the incidence of stomach ulcers.

4.3. REPRODUCTIVE/DEVELOPMENTAL STUDIES—ORAL AND INHALATION

Reproductive/developmental toxicity studies are not available in humans by the oral or inhalation routes of exposure. No reproductive/developmental animal toxicity studies were identified by the inhalation route of exposure. Oral reproductive and developmental studies in experimental animals are summarized in Table 4-3.

4.3.1. Studies in Rats

Hardy et al. (2002) conducted a developmental toxicity study in rats by using a composite of three lots of a commercial flame retardant (97.34% decaBDE and 2.66% nonaBDE and octaBDE) produced by three manufacturers. In this study, Sprague-Dawley rats (25 mated females per dose group) were administered decaBDE in corn oil by gavage at doses of 0, 100, 300, or 1,000 mg/kg-day during gestation days 0 through 19. Dams were observed daily for morbidity, mortality, and signs of injury. Maternal body weight, body-weight gain, and food consumption were monitored. Dams were sacrificed on day 20 of gestation, and liver weights, gravid uterine weights, and the number of corpora lutea, implants, fetuses, and resorptions were recorded. The placenta and fetuses were examined for gross abnormalities, and histologic examinations were performed.

All dams survived decaBDE treatment until scheduled sacrifice. There were no adverse treatment-related effects observed in maternal clinical findings, body weight, or body-weight gain. Although a slight but statistically significant increase in food consumption was observed at 1,000 mg/kg-day at time intervals up to day 12 of gestation, the authors did not consider this indicative of an adverse effect of treatment.

Table 4-3. Oral developmental and reproductive studies for decaBDE in laboratory animals

Study	Species, sex, and sample size	Route, dose, and duration	Observed effects	NOAEL	LOAEL	Comments
Hardy et al. (2002)	Rat, Sprague-Dawley, pregnant female, 25/dose group	Gavage (97.34% purity); 0, 100, 300, or 1,000 mg/kg-day; gestation days 0–19	No statistically significant maternal or developmental treatment-related effects	1,000 mg/kg-day	Not identified	
Viberg et al. (2007)	Rat, Sprague-Dawley, male, 20 rats from 3–5 litters/treatment group	Single dose gavage (>98% purity in 20% fat emulsion); 0, 6.7, or 20.1 mg/kg on PND 3	Significant dose-related disruption in habituation (changes in locomotion, rearing, and total activity) at 2 months in rats, following exposure to 6.7 and 20.1 mg/kg on PND 3	Not identified	6.7 mg/kg	Single dose experiment
Viberg et al. (2003a)	Mouse, NMRI, male, 10 mice from 3–5 litters/ treatment group	Single oral gavage (>99% purity in 20% fat emulsion); 0, 2.22, or 20.1 mg/kg (PNDs 3 and 19); 0, 1.34, 13.4, or 20.1 mg/kg (PND 10)	Significant dose-related disruption in habituation (changes in locomotion, rearing, and total activity) at 2, 4, and 6 months in mice, following exposure to 20.1 mg/kg on PND 3	2.22 mg/kg	20.1 mg/kg	Single dose experiment
Tseng et al. (2006)	Mouse, CD-1, male, 50/dose group	Oral gavage (98% purity in corn oil); 0, 10, 100, 500, or 1,500 mg/kg-day; PNDs 21–70	Reduced amplitude of sperm lateral head displacement, reduced sperm mitochondrial membrane potential, increased sperm H_2O_2 generation	100 mg/kg-day	500 mg/kg-day	
Rice et al. (2007)	Mouse, C57BL6/J, 3 males and 3 females from 11–13 litters/treatment group	Micropipette administration (99.5% purity in 20% fat emulsion); 0, 6, or 20 mg/kg-day; PNDs 2–15	Decreased number of male and female pups performing the palpebral reflex on PND 14, increased struggling behavior on PND 20, effects on grip strength on PNDs 14 and 16, effects on locomotor activity on PND 70	Not identified	6 mg/kg-day	

No statistically significant differences were observed in maternal absolute or relative liver weights between treatment and control groups. At necropsy, gross examination of the dams revealed no adverse effect of treatment with decaBDE. Number of dams with viable fetuses, mean number of corpora lutea, number of implantation sites, percent preimplantation loss per dam, number of viable fetuses, and gravid uterine weights were not adversely affected by decaBDE treatment.

A statistically significant increase in the mean number of early resorptions per dam was observed in the 1,000 mg/kg-day group compared to controls. Based on the lack of a consistent dose response for this effect (the mean number of early resorptions per dam was 0.6, 0.6, 0.5, and 1.4 at 0, 100, 300, and 1,000 mg/kg-day, respectively), lack of a statistically significant positive trend associated with the effect, and the historically high incidence of this effect (0.5–1.4) for the laboratory, these effects are not considered to be of toxicological significance. Examination of the results indicated a marginal increase in the postimplantation loss/dam of 7 and 9% at 300 and 1,000 mg/kg-day, respectively, compared with 4% in controls and at 100 mg/kg-day. However, this effect was not associated with a statistically significant positive trend. A slight, but statistically not significant, decrease in the percentage of viable fetuses per implant was seen
(96, 96, 93, and 91% in the control, 100, 300, and 1,000 mg/kg-day groups, respectively). Fetal body weights, crown-rump ratio, and fetal sex ratio were not different between treatment and control groups. No adverse decaBDE treatment-related effects were identified during fetal external, skeletal, or visceral examinations. DecaBDE treatment, therefore, did not produce any evidence of maternal or developmental toxicity up to the highest dose tested of 1,000 mg/kg-day. The NOAEL for maternal and developmental toxicity in this study was 1,000 mg/kg-day, the highest dose tested.

BDE-209 (>98% purity) in a fat emulsion was administered by gavage to 3-day-old Sprague-Dawley rats at 0, 6.7, or 20.1 mg/kg (Viberg et al., 2007). A total of 20 rats were picked from three to five different litters in each treatment group. Motor activity was measured for a 60-minute period, divided into three 20-minute periods, in rats at the age of 2 months. Motor activity tests measured locomotion (horizontal movement), rearing (vertical movement), and total activity (all types of vibration within the test cage [i.e., those caused by rat movements, shaking/tremors, and grooming]). There were no clinical signs of toxicity in the BDE-209-treated rats at any given time during the experimental period, nor was there any significant difference in body-weight gain or adult weight between controls and rats treated with BDE-209. In control rats, there was a distinct decrease in locomotion, rearing, and total activity at 2 months of age, indicating habituation in response to the diminishing novelty of the test chamber over the 60-minute test period. Habituation is defined as the ability of the animals to adapt to a new environment and is characterized as initial investigation and exploration of their surroundings followed by gradual acclimatization and acceptance of the new area. Two-month-old rats exposed to 20.1 mg/kg BDE-209 on PND 3 displayed significantly less activity for all three behavioral variables during the first 20-minute test period compared with controls, while during the third 20-minute period (40–60 minutes) they were significantly more active than the control animals. Rats receiving the low dose of BDE-209 (6.7 mg/kg) showed significantly increased locomotion activity during the second 20-minute period, significantly decreased rearing activity during the first and second 20-minute periods, and significantly higher total activity during the first and second 20-minute periods compared with the control rats. The LOAEL in this study was 6.7 mg/kg for significant changes in spontaneous motor behavior (locomotion, rearing, and total activity) in 2-month-old rats given BDE-209 on PND 3.

Immediately after the spontaneous behavior tests, nicotine-induced behavior was studied to determine whether changes in spontaneous behavior in adult rats neonatally exposed to BDE-209 included effects on development of the cholinergic system and thereby altered the response in the adult animal to the cholinergic agent nicotine (Viberg et al., 2007). The rats were given a single subcutaneous injection of 80 µg nicotine base/kg, a dose known to cause an increase in activity in experimental animals, and were immediately tested again for nicotine-induced motor behavior with regard to locomotion, rearing, and total activity during another 60-minute period divided into three 20-minute periods.

Pair-wise testing between the nicotine-injected and saline-injected rats showed, as expected, a significant increase in response to nicotine in the neonatally vehicle-treated rats during the first 20-minute period (60–80 minutes) for all three variables (locomotion, rearing, and total activity). In contrast, the nicotine-injected rats exposed to 20.1 mg/kg of BDE-209 on PND 3 showed significantly decreased activity for all three tests (locomotion, rearing, and total activity) during the first 20-minute period (60–80 minutes) compared with the rats neonatally exposed to the high BDE-209 dose and injected with saline. The authors concluded that neonatal exposure to BDE-209 on PND 3 affects adult spontaneous behavior and also affects the cholinergic system, seen as changes in the adult rats' response to the cholinergic agent nicotine.

4.3.2. Studies in Mice

Viberg et al. (2003a) assessed the potential of decaBDE to affect the developing central nervous system. The neurotoxic effects of decaBDE on spontaneous motor behavior of NMRI male mice were investigated in adult animals exposed to a single oral dose as neonates. Uptake of radiolabel by the brain of the neonatal mice orally administered ^{14}C-labeled BDE-209 on PND 3, 10, or 19 (i.e., at different stages of neonatal mouse brain development) was also measured to determine if there were age-related differences in tissue toxicokinetics that might correlate with the neurodevelopmental effects evaluated.

In this behavioral study, 3-day-old and 19-day-old male mice were given a single dose of 0, 2.22, or 20.1 mg/kg body weight decaBDE (purity estimated to be >99%) in a 20% (weight/weight) emulsion vehicle of egg lecithin-peanut oil and water. Ten-day-old mice received 0, 1.34, 13.4, or 20.1 mg/kg. The spontaneous behavior test (measuring locomotion, rearing, and total activity) was conducted in 10 mice randomly selected from the litters in each treatment group at 2, 4, and 6 months of age. There were three to five litters (four to seven males per litter) in each of the dose groups. The behavior variables were measured for a 60-minute period divided into three consecutive 20-minute periods. In order to study time-dependent changes in habituation, an habituation ratio was calculated by dividing the motor behavior measures from the 40- to 60-minute observation period by those from the 0- to 20-minute period and multiplying by 100 for each of the three different variables: locomotion, rearing, and total activity. The habituation ratios from 2-, 4-, and 6-month-old mice within each treatment group were then compared. An increase in habituation ratio indicates decreased capability to habituate to a novel environment. Data for the three spontaneous behavior variables and habituation ratio are only available in graphic form and could not be used for quantitative assessment.[1]

Treatment with decaBDE caused no clinical signs of toxicity at any time during the experimental period. Body weight and body-weight gain were not significantly different between decaBDE- and vehicle-treated mice in the three different age groups. Control mice treated on PND 3, 10, or 19 exhibited normal habituation profiles. Pair-wise testing between adult mice exposed to 20.1 mg/kg on PND 3 and control groups indicated significant changes in all three spontaneous behavior variables at 2, 4, and 6 months of age. For the first 20 minutes, mice receiving 20.1 mg/kg displayed significantly less activity for locomotion, rearing, and total activity compared with controls. During the third 20-minute period, exposure of mice to 20.1 mg/kg on PND 3 caused significantly more activity for locomotion, rearing, and total activity than the controls at 2, 4, and 6 months. The only effect noted in mice exposed to 2.22 mg/kg was a significant decrease in total activity in the first 20-minute test period compared with the controls at 2 months of age. However, total activity returned to control level during the third 20-minute period. The lower dose of 2.22 mg/kg did not elicit any significant differences in these three variables compared with controls at 4 months of age. Lower activity was observed at 2.22 mg/kg during the first 20-minute period for the rearing variable at 6 months of age compared with controls, again returning to control level during the third 20-minute period. Mice exposed neonatally up to 20.1 mg on either PND 10 or 19 did not show any significant differences in any of the variables after 2, 4, or 6 months compared with controls. The authors indicated that the absence of effects on spontaneous activity in mice treated on PNDs 10 and 19 suggests that there is a critical window for the induction of the observed behavioral disturbances.

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[1] Attempts to obtain numerical values and other information on the data from the authors were not successful.

The habituation ratio calculated from the three spontaneous motor behavior variables (locomotion, rearing, and total activity) significantly increased after 2, 4, and 6 months of age in mice exposed on PND 3 to 20.1 mg/kg. Mice exposed on PND 3 to 2.22 mg/kg did not show a significant decrease in habituation capability with age. The decrease observed in the habituation capability in the adult mice exposed neonatally to the high dose indicated that the neurotoxic effect of neonatal decaBDE exposure was persistent and also worsened with age. The NOAEL in this study was 2.22 mg BDE-209/kg, and the LOAEL was 20.1 mg/kg for significant changes in spontaneous motor behavior and decreased habituation capability for locomotion, rearing, and total activity, worsening with increasing age.

Neonatal exposure to ^{14}C-decaBDE (specific activity 17.5 mCi/mmol) in mice on PND 3, 10, or 19 revealed that the labeled substance was absorbed and distributed to the brain, heart, and liver. However, the amounts in the liver 24 hours after dosing on PNDs 3, 10, and 19 were 12.6, 9.4, and 5.8%, respectively. The lower amount of BDE-209 measured as the dosing day occurred later suggests that gastrointestinal absorption may have decreased as the gastrointestinal tract matured over the first 19 days after birth. Only a small fraction of the dose reached the brain or heart 24 hours after dosing, especially with dosing on day 19 (see Viberg et al. [2003a] in section 3.2.2). However, results indicated that the amount of radioactivity increased significantly in the brain over a 7-day period in animals exposed on PNDs 3 and 10 but not in those exposed on PND 19. The radioactivity in the liver and heart was the same or decreased during the 7-day period following oral administration on PNDs 3, 10, and 19. The observed increase in radioactivity in the brain over the 7-day period suggests slow transport of decaBDE and/or its metabolites to the brain, which may account for the fact that administration on day 3 caused a more significant impact on habituation than administration on PND 10 or 19. The radiolabel data showed that the amount of decaBDE in the brain 24 hours after dosing on PNDs 3, 10, and 19 was 0.5, 0.4, and 0.06%, respectively. The radioactivity was significantly greater 7 days after BDE-209 administration on PNDs 3 and 10 compared with 24 hours after administration. The amount of radioactivity measured in the brain 7 days after dosing on PNDs 3 and 10 (PNDs 10 and 17) was 0.7 and 1.1%, respectively. There was no change in the amount of radioactivity measured in the brain of animals 7 days after dosing on PND 19.

Rice et al. (2007) examined the effects of BDE-209 (99.5% purity) on developmental milestones, sensorimotor behaviors, serum T_4 levels, and locomotor activity in male and female C57BL6/J mice administered doses of 0, 6, or 20 mg/kg-day. The BDE-209, in a 20% egg lecithin/peanut oil/water emulsion, was administered to the pups from PNDs 2–15 by using a micropipette to avoid gavaging neonatal animals. There were no delays in postnatal developmental milestones (pinna detachment, incisor eruption, eye opening, vaginal opening, or testes descent) from BDE-209 treatment in male or female mice. There were no effects of exposure on anogenital distance or crown-rump length.

The authors developed a special functional observational battery (FOB), suitable for neonatal mice, to examine a series of home-cage, reflexive, and sensorimotor behaviors, measured on PND 14, 16, 18, or 20. Three of the FOB endpoints were affected by BDE-209 exposure: palpebral reflex, forelimb grip, and struggling behavior during handling. On PND 14, significantly fewer male and female pups in the 6 and 20 mg/kg-day groups performed the palpebral reflex compared with controls. On PNDs 14 and 16, fewer male pups in the 20 mg/kg-day group performed an effective forelimb grip compared with same-sex controls. Male and female pups in the 6 mg/kg-day group struggled significantly more on PND 20, while they were being handled for the FOB, compared with controls and the high-dose group.

Rice et al. (2007) also examined the locomotor activity of male and female mice in a novel environment over a 2-hour period on PND 70 and at approximately 1 year of age (one male and one female from each of 9–13 litters were evaluated). Locomotor activity declined over the course of the 2-hour assessment in PND 70 males and in females in the control and treated groups. However, the rate of decline was significantly different ($p = 0.04$) in male mice exposed to 6 and 20 mg/kg-day compared with control animals, an effect that was most pronounced in the high-dose males during the first 1.5 hour of the 2-hour activity session. There was a non-dose-related decline in the locomotor activity in the female mice during the 2-hour activity session. Unlike the males, they became hypoactive compared with the controls. There was no effect of BDE-209 treatment on the locomotor activity of the 1-year old male and female mice.

The effect of BDE-209 treatment on serum T_4 in PND 21 offspring was also investigated in this study. A dose-related reduction in serum T_4 in comparison with controls occurred in males but not in females.

The LOAEL in this study was 6 mg/kg-day, the lowest dose tested, for decrease in the percent of male and female pups performing the palpebral reflex on PND 14, for increased struggling behavior of male mice on PND 20, for decreased T_4 levels in male mice, and for effects on locomotor activity of male mice on PND 70.

Tseng et al. (2006) studied the effects of BDE-209 on mouse sperm function, DNA content, and histopathology of the testes. CD-1 male mice (50/dose group) were fed decaBDE (98% purity) by gavage in corn oil at 0, 10, 100, 500, or 1,500 mg/kg-day from PNDs 21–70. Body weight, body-weight gain, and absolute and relative weights of the testis, epididymis, cauda epididymis, and seminal vesicle of treated animals were not significantly different from controls at sacrifice on PND 71. Morphology of the testicular tissues appeared normal in all treated groups compared with controls. DNA content in testis cells was unaffected by treatment with BDE-209. No significant differences in sperm motility (expressed as the ratio between the number of motile sperm and total number of sperm), sperm count, or morphology were seen among the groups exposed to BDE-209 and the controls. Sperm motion velocity parameters were measured, including curvilinear velocity, straight-line velocity, and amplitude of the lateral head displacement (ALH). The only effect seen on sperm motion velocity was a significant decrease in ALH at 500 and 1,500 mg/kg-day. Significant increase in the generation of hydrogen peroxide in the sperm of sexually mature mice occurred at 500 and 1,500 mg/kg-day. The mitochondrial membrane potential (MMP) of sperm cells, a predictor of sperm fertility potential, was assessed using a lipophilic cationic compound, JC-1, which possesses the ability to differentially label mitochondria with high and low membrane potential (Gravance et al., 2001). Mice exposed to 500 and 1,500 mg/kg-day were found to have a significant decrease in high MMP sperm. In addition, the MMP was negatively and significantly associated with the generation of sperm hydrogen peroxide. The NOAEL in this study was 100 mg/kg-day and the LOAEL 500 mg/kg-day for decrease in ALH and MMP and increased generation of hydrogen peroxide in the sperm of adult mice.

4.4. OTHER ENDPOINT-SPECIFIC STUDIES

4.4.1. Receptor Site Interactions

Some studies of halogenated aromatic compounds show that they exert an influence on cells by interacting with membrane receptor sites and activating cellular transcription factors. Transcription factor complexes then initiate DNA synthesis, allowing the cell to respond to the extracellular signal by producing a series of mRNAs that in turn produce a variety of proteins. This process is termed signal transduction. The structural similarities between PBDEs and polychlorinated biphenyls (PCBs) suggest that PBDEs might activate the aryl hydrocarbon receptor (AhR) and the estrogen receptor (ER). Based on the data from the well-studied PCBs and dioxins, the activation of these receptors is associated with immunosupression, reproductive effects, and carcinogenesis (Klaassen, 1996; Bock, 1994), all endpoints of interest for PBDEs. Studies of receptor interactions of BDE-209 with the AhR, ER, pregnane X receptor (PXR), and steroid X receptor (SXR) are summarized in the sections that follow. As a group, these studies indicate that the ability of BDE-209 to activate signal transduction responses via the receptors studied is minimal or negligible.

4.4.1.1. *Aryl Hydrocarbon Receptor Studies*

Although in vivo studies investigating mechanisms of liver toxicity in animals have not been identified, several in vitro systems have evaluated the ability of decaBDE to interact with the AhR by using liver tissues or cell lines. Brown et al. (2004) investigated the potential of decaBDE to bind to and activate the AhR (using a gel retardation assay) and the ability of decaBDE to induce the expression of dioxin-responsive genes (using the reporter gene based

Chemical-Activated Luciferase eXpression [CALUX] assay). The decaBDE used in this study was 85.5% purity, and the identities of the other components present in the preparation were not reported. Incubation of decaBDE with hepatic cytosol prepared from guinea pigs and subsequent incubation with [^{32}P]-labeled dioxin-responsive element (DRE)-containing oligonucleotide, followed by resolution of the ligand:AhR:[^{32}P]DRE complex by gel retardation analysis, indicated that decaBDE (20 μM) stimulated AhR-DNA binding but to a much lower level (26%) than 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). DecaBDE demonstrated some activity in the CALUX assay. Based on the results from gel retardation and reporter gene assays, decaBDE may induce AhR-dependent DNA binding and gene expression but with very low potency if the activity observed is solely attributable to decaBDE. However, the low but measurable activity may have been caused by contaminants since the test material was impure.

The possible dioxin-like effects of decaBDE or induction of genes that encode metabolizing enzymes have also been investigated by Peters et al. (2004). AhR-mediated induction of CYP-1A1 and -1B1 were studied in human breast carcinoma MCF7 cells by using EROD activity as a marker for CYP-1A1 and -1B1 activity. DecaBDE (>98% purity) did not induce EROD activity and, therefore, was not found to be an AhR agonist in these cells incubated for 72 hours with decaBDE at concentrations that were not cytotoxic (up to 10 μM). Additionally, exposure of the cells to decaBDE did not induce mRNA levels of CYP-1A1 or -1B1, indicating no effect of decaBDE on AhR gene expression.

Villeneuve et al. (2002) evaluated the dioxin-like potency of decaBDE (99% purity) at environmentally relevant concentrations (up to 500 ng/mL) by using in vitro luciferase assays with H4IIE-luc recombinant rat hepatoma cells. DecaBDE did not induce AhR-dependent gene expression. The authors calculated that most PBDEs, including decaBDE, were at least 10,000 times less potent than TCDD for inducing AhR-mediated responses in vitro.

The affinity of decaBDE for rat hepatic AhR was evaluated through competitive binding assays (Chen et al., 2001). Results indicated that decaBDE has no AhR-binding activity. The ability of decaBDE to induce hepatic CYP-450 enzyme activity by means of EROD assays in human, rat, chick, and rainbow trout cells was also determined in this study. Incubation of decaBDE (of unspecified purity) with cultures of primary rat hepatocytes, primary chick embryo hepatocytes, two human cell lines (hepatoma HepG2 and intestinal Caco-2), and one rat cell line (hepatoma H4IIE) showed that decaBDE did not induce EROD activity in any cell line tested. Moreover, decaBDE was almost completely inactive in a gel retardation assay, suggesting that decaBDE did not activate the AhR.

Pullen et al. (2003) investigated the effect of decaBDE on CYP-450 activity in mouse hepatocytes. Incubation of decaBDE (of unspecified purity) with hepatocytes isolated from C57BL/6 mice for 24 hours did not induce CYP-1A1 (measured as EROD activity), indicating that decaBDE does not act as a specific ligand for the AhR and, thus, exerts no effect via the

AhR pathway as do many of the polycyclic aromatic hydrocarbons. Together, these studies suggest that decaBDE has very limited potential to activate the AhR signal transduction pathway, which is an important step in the mode of action through which many persistent aromatic hydrocarbons impact cell regulation and cell maintenance (Klaassen, 1996).

4.4.1.2. *Estrogen Receptor Studies*

ER-mediated (estrogenic) effects of decaBDE at environmentally relevant concentrations were investigated by Villeneuve et al. (2002) in an in vitro luciferase assay system. Incubation of decaBDE (99% purity) at concentrations up to 500 ng/mL with MVLN recombinant human breast carcinoma cells for 72 hours showed that decaBDE did not exhibit estrogenic effects. Most PBDEs, including decaBDE, were at least 50,000 times less potent than 17β-estradiol (E2) for inducing ER-mediated gene expression. This study also examined the ability of decaBDE to displace E2 or testosterone from serum proteins in a competitive hormone displacement assay. Incubation of decaBDE at concentrations up to 2.5 μg/mL in the presence of ^{3}H-estradiol or ^{3}H-testosterone and hormone-stripped carp serum for 15 hours indicated that decaBDE did not cause any significant displacement of these hormones in vitro. These results suggest that decaBDE and other PBDEs are not likely to elicit E2-mediated gene expression at the exposure levels currently observed in fish and wildlife.

4.4.1.3. *Other Receptors*

Pacyniak et al. (2007) conducted a study of the PXR and its human counterpart SXR by using HepG2 cells transvested with the appropriate complementary DNA (cDNA), the receptor response elements, and a luciferase reporter vector. The cultured cells were exposed to 0, 0.1, 1, 10, or 100 μM concentrations of BDE-209. With the PXR there was a very slight dose-related increase in relative luciferase activity that achieved significance for only the highest concentration. With the SXR, there was no impact of luciferase for any concentration other than the 100 mM preparation. Accordingly, BDE-209 appears to be a weak inducer for PXR and SXR. The authors also compared the response in PXR knock-out mice (10–12 weeks old) with the wild-type mice and found that CYP-3A11 was induced to a greater extent in the wild-type animals, indicating that BDE-209 seems to be a ligand for the PXR. However, even in the knock-out mice, some CYP-3A11 protein was identified, suggesting that the PXR was not the only receptor affected by BDE-209. The authors suggested that the persisting CYP-3A11 protein could be related to activation of the constitutive androstane receptor (CAR).

4.4.2. Immunological Studies

No in vivo studies that specifically evaluated the immunosuppressive effects of decaBDE have been identified. However, in chronic dietary studies, decaBDE has been found to induce histological changes in lymphoid organs, including the spleen (fibrosis) and mandibular lymph nodes (hyperplasia) in male rats at a dose of 2,240 mg/kg-day (NTP, 1986). Although these histopathological changes may play an important role in flagging decaBDE for immunotoxicity, they are at the high end of the spectrum of doses evaluated, and the lack of studies to investigate the functional effects on immune cells from exposure to decaBDE precludes complete assessment of its immunotoxic potential.

Only one study investigated the immunotoxic effects of decaBDE on intact lymphocytes. Pullen et al. (2003) isolated splenocytes from C57BL/6 mice and incubated the cells in culture with decaBDE (purity not specified). DecaBDE was not cytotoxic to these cells at 3 μmol/L. Treatment of cells for 48 hours with 3 μmol/L decaBDE did not cause attenuation of interleukin-2-receptor α chain (CD25) expression (evaluated by immunohistochemistry and confocal microscopy or laser scanning cytometry). The lack of attenuation of CD25 expression suggests that decaBDE is not likely to alter a surface marker (which is essential for lymphocyte proliferation during immune response) and may not affect the immune system in an immunosuppressive manner. Pullen et al. (2003) also evaluated the potential of decaBDE to alter cytokine production. Results showed that decaBDE did not have any effect on the production of the cytokines IFN-γ, IL-2, IL-6, and IL-10, indicating that decaBDE does not interfere with the cells' ability to synthesize protein.

4.4.3. Genotoxicity

In vitro studies were conducted to evaluate the mutagenic potential of decaBDE (NTP, 1986). DecaBDE was tested in *Salmonella typhimurium* TA98, TA100, TA1535, or TA1537 strains up to 10,000 μg/plate in the presence or absence of exogenous metabolic system (S9 fractions) prepared from the livers of Aroclor 1254-induced male Sprague-Dawley rats or male Syrian hamsters. Results indicated that decaBDE was not mutagenic in the salmonella assay systems.

The mutagenicity of decaBDE at doses of up to 10 μg/mL was evaluated in L5178Y/TK$^{+/-}$ mouse lymphoma cell assay system in the absence or presence of S9 prepared from the livers of Aroclor 1254-induced male F344/N rats. DecaBDE did not induce mutagenic potential in this assay system. DecaBDE at doses up to 500 μg/mL did not induce sister-chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in the absence or presence of S9 prepared from the livers of Aroclor 1254-induced male Sprague-Dawley rats (NTP, 1986).

Results from these studies provide evidence that parent decaBDE in the presence or absence of an exogenous liver metabolic system does not react directly or indirectly with DNA to cause gene mutations, DNA damage, or chromosomal effects.

4.5. SYNTHESIS OF MAJOR NONCANCER EFFECTS

4.5.1. Oral

Several studies have been conducted to evaluate the effects of decaBDE and to elucidate its mode of action. Long-term dietary studies conducted by NTP (1986) have identified nonneoplastic liver and thyroid histopathology, such as liver thrombosis and degeneration in male rats, and liver granulomas, centrilobular hypertrophy, and thyroid follicular cell hyperplasia in male mice.

Neurobehavioral developmental effects on habituation were seen in adult male rats (Viberg et al., 2007) and adult male mice (Viberg et al., 2003a) given a single dose of BDE-209 during the postnatal period. Male and female mice pups given BDE-209 during the neonatal period showed early effects on palpebral reflex, forelimb grip, and struggling behavior. Locomotor activity was also affected in young adult male mice (Rice et al., 2007).

Behavioral disturbances observed in the mature rats and mice exposed to decaBDE as neonates (Rice et al., 2007; Viberg et al., 2007, 2003a) raise concern about possible developmental neurotoxicity in children. In the study by Viberg et al. (2003a), neonatal male mice were given a single dose of decaBDE (up to 20.1 mg/kg) in a fat emulsion on PNDs 3, 10, or 19 and spontaneous motor behavior tests (measuring locomotion, rearing, and total activity) were conducted in the mice at 2, 4, or 6 months of age. In addition, an habituation ratio was also determined for each behavior variable at the tested ages. Exposure of 3-day-old mice to 20.1 mg/kg decaBDE resulted in significant dose-related changes in all three spontaneous behavior variables at 2, 4, and 6 months of age. However, adult mice exposed neonatally up to 20.1 mg on either PND 10 or 19 did not show any significant differences in any of the variables after 2, 4, or 6 months compared with controls. In the study in rats (Viberg et al., 2007), significant dose-related disruption in habituation (changes in locomotion, rearing, and total activity) was observed in 2-month-old rats, following exposure to BDE-209 at 6.7 and 20.1 mg/kg on PND 3.

Rice et al. (2007) used a similar approach in evaluating locomotor activity in groups of 9–13 male and female C57BL6/J mice exposed to 6 or 20 mg/kg-day BDE-209 from PNDs 2–15 and observed after placement in a novel environment on PND 70 during a 2-hour period. The exposed males showed greater activity than the controls throughout the observation period. Early in the period, the exposed male mice were hyperactive compared with controls; the difference between the exposed animals and controls declined with time but locomotor activity remained greater than that for the controls at the end of the 2-hour observation period. In the case of the females, the activity of all groups was similar for the first 45 minutes of exposure but the females became less active than the controls thereafter. The linear slope for the decline in activity among the exposed males was significantly different from that of controls; the 20 mg/kg group was affected to a greater extent than the 6 mg/kg group. The females on PND 70 and both sexes when examined at 1 year after birth did not display similar dose-related differences in locomotor activity.

Rice et al. (2007) also examined a number of developmental and behavioral parameters during the dosing period and for five days after dosing ceased. BDE-209 exposure did not impact the developmental endpoints evaluated (pinnae detachment, incisor eruption, eye opening, vaginal opening, testes descent). The behavioral parameters studied were selected as measures of home-cage, motor, and sensorimotor behaviors. There was no apparent impact on most measures of behavior; however, palpebral reflex, forelimb grip, and struggling during handling appeared to be impacted by BDE-209 exposure. There was a significantly poorer performance of the 20 mg/kg-day group in the palpebral reflex test on PND 14 and in the grip test (males only) on PND 16. On PND 20, the struggling behavior of the group exposed to 6 mg/kg was significantly increased compared with the controls and 20 mg/kg-day group.

The most striking dose-related trend in the Rice et al. (2007) study was the locomotive activity profile of males at PND 70. The direction of this trend differed from that observed by Viberg et al. (2007, 2003a). In the Rice et al. (2007) study, activity in the exposed and control mice decreased across the observation period, while in the Viberg et al. (2007, 2003a) studies activity increased across the observation period for the exposed animals compared with the controls. However, the exposure and testing conditions varied between the two studies and, thus, the two sets of results are not directly comparable.

4.5.2. Inhalation

No data are available on the toxicity of decaBDE by the inhalation route of exposure.

4.5.3. Mode-of-Action Information

Impaired development of the cholinergic system during the postnatal "brain growth spurt" period has been offered as a plausible hypothesis for the observed neurodevelopmental impact of the PBDEs on adult responses to a novel environment (Viberg et al., 2007, 2003b). The authors described a critical window of vulnerability in development of the cholinergic system during postnatal development that in mice occurs in the first few weeks after birth with a peak at PND 10 (Viberg et al., 2003b). They hypothesize that any agent that caused a deficit in cholinergic receptors during this period could cause a hypoactive response to cholinergic stimulants, including exposure to a novel environment in adulthood.

Viberg et al. (2007) tested this hypothesis in Sprague-Dawley rats. Two-month-old rats that had been exposed to vehicle, 6.7 mg/kg, or 20 mg/kg BDE-209 on PND 3 were given a subcutaneous injection of nicotine or saline solution. The vehicle control animals and animals in the 6.7 mg/kg dose group receiving the nicotine demonstrated the typical hyperactive response of mature rats when compared with the saline-injected rats during the 60–80 minute observation period. Those given the 20.1 mg/kg dose were markedly hypoactive compared with the saline controls. These observations provide some support for the hypothesis that impaired prenatal development of the cholinergic system may play a role in the habituation deficits observed in adult rats and mice that were prenatally exposed to decaBDE during the critical window for system development.

Other studies by the Eriksson/Viberg research team using PBDE compounds with four, five, and six bromines have shown effects on locomotion and habituation that are similar to those observed for the deca compound. However, in the study of BDE-99, when the timing of exposure was varied, the window of greatest vulnerability occurred on day 10 rather than on days 3 or 19 (Eriksson et al. 2002). Thus, the results for BDE-99 are different from those for decaBDE reported in Viberg et al. (2003a). However, the data from the radiolabel component of the study provide a rationale for the difference in the apparent window of vulnerability. Two contributing factors are observed. First, absorption from the gastrointestinal tract decreases as the neonatal mice age during their first few weeks of life. Thus, less of the decaBDE reaches the liver for distribution on days 10 and 19 than on day 3. Secondly, distribution to the brain is slow. The amount of radiolabel in the brain is higher (0.7%) when measured 7 days after dosing on PND 3 than when measured 24 hours after dosing (0.5%). The radioactivity measured 7 days after dosing was also higher than when measured 24 hours after dosing on PND 10 (0.4% at 24 hours; 1.1% at 7 days). Less than 0.1% of the label reaches the brain when the compound is administered on day 19. While evidence exists that demonstrates BDE-209, as well as other PBDEs, interact at the neurological level, data are inadequate to determine the mode of action for BDE-209.

DecaBDE caused thyroid gland follicular cell hyperplasia and thyroid tumors in male mice, effects that are indicative of thyroid toxicity (NTP, 1986). Based on these effects, decaBDE may share the general property of organohalogen compounds in which in vivo exposure in rodents results in reduction of serum total and free thyroid hormone (T_4) levels (Legler and Brouwer, 2003). Thyroid hormone disruption has been hypothesized to arise from at least two different mechanisms, one of which is the induction of liver enzymes of different enzyme families, including CYP-1A1 and CYP-2B (McDonald, 2002). Induction of liver UDPGTs may increase the rate of T_4 conjugation and excretion, which is believed to be a mechanism for TCDD-induced thyroid effects. An increase in the metabolism of T_4 will result in enhanced excretion and thus a drop in its circulating levels. The other mechanism involves alteration of thyroid homeostasis through hormone mimicry. Potential thyroid toxicants may be metabolized by liver enzymes to metabolites that compete with the thyroid transport protein, transthyretin, a key protein involved in the transport of T_4 through the blood and into the developing tissues in rodents.

Zhou et al. (2001) evaluated the interference of decaBDE with thyroid hormone homeostasis in weanling rats exposed to decaBDE (>98% purity) up to 100 mg/kg-day for 4 consecutive days. Results indicated that decaBDE did not affect hepatic enzyme activities or serum T_4, T_3, TSH, and hepatic UDPGT activity at doses up to 100 mg/kg-day. Rice et al. (2007) also evaluated T_4 levels in the blood of C57BL6/J mice (1 male, 1 female/litter) on PND 21 following exposure to 0.6 or 20 mg/kg-day BDE during PNDs 2–15. In this instance, there was a dose-related reduction in the T_4 levels for males but not females. Despite the possibility of thyroid hormone involvement in the neurodevelopmental impact of BDE-209 on the habituation response in male mice exposed to a single dose on PND 3, there are no mode-of-action data that link thyroid hormones to the neurobehavioral observations reported by Viberg et al. (2003a).

In the chronic dietary studies conducted by NTP (1986), decaBDE has been found to induce histologic changes in lymphoid organs, including the spleen (fibrosis) and mandibular lymph nodes (hyperplasia), in rats. These histopathologic changes could flag decaBDE as a potential immunotoxicant. No in vivo functional immunotoxicity studies were identified. Results from an in vitro study investigating the immunotoxic effects of decaBDE indicated that decaBDE did not show any attenuation of CD25 expression or changes in cytokine production (Pullen et al., 2003). As such, decaBDE is unlikely to affect the immune system in an immunosuppressive manner.

Several in vivo and in vitro studies have evaluated decaBDE for its potential to activate the AhR signal transduction pathway and to induce gene expression, resulting in increased phase I and phase II metabolism. Taken together, the in vivo and in vitro studies suggest that decaBDE has very low or no potential to bind the AhR. The inability of decaBDE to elicit CYP-450 induction or AhR binding and gene expression, indicating lack of potential to activate the AhR signal transduction pathway, suggests that decaBDE may cause liver toxicity through a different mechanism and that the observed liver effects are not an adaptive effect related to enzyme induction. Results from the Morck et al. (2003) study indicated high concentration of tissue-bound radioactivity in the liver, and the radioactivity was assumed to be bound to macromolecules. The authors asserted that binding occurred via reactive metabolites. Formation of such metabolites may be responsible for the liver toxicity observed on exposure to decaBDE. However, the enzymes responsible for decaBDE metabolism and reactive intermediates have not been identified. The existing data show tissue binding and are therefore not adequate to elucidate a potential role in the mode of action.

A number of studies have also indicated that brominated flame retardants may interfere with estrogen pathways by binding to and activating ERs (Legler and Brouwer, 2003). No in vivo studies were identified that evaluated the specific estrogenic effects of decaBDE. Furthermore, specific effects attributable to estrogenic dysregulation were not identified in the available animal studies, although some developmental toxicity endpoints were observed. Mechanistic studies do not support effects of decaBDE on ER pathways.

4.6. EVALUATION OF CARCINOGENICITY

4.6.1. Summary of Overall Weight of Evidence

Under the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a), the descriptor "suggestive evidence of carcinogenic potential" is appropriate for decaBDE. This descriptor of the database is appropriate when the weight of evidence is suggestive of carcinogenicity and a concern for potential carcinogenic effects in humans is raised, but the data are judged not sufficient for a stronger conclusion. This descriptor covers a spectrum of evidence associated with varying levels of concern for carcinogenicity, ranging from a positive cancer result in the only study on an agent to a single positive cancer result in an extensive database that includes negative studies in other species.

The weight of evidence of human carcinogenicity of decaBDE is based on (1) no studies of cancer in humans exposed to decaBDE; (2) a statistically significant increase in incidence of neoplastic nodules in the liver of low- and high-dose male rats and high-dose female rats; (3) a significantly increased incidence of hepatocellular adenoma or carcinoma (combined) in male mice at the low dose and marginally increased incidence at high dose; (4) a nonsignificantly increased incidence of hepatocellular adenoma or carcinoma (combined) in female mice; (5) a slightly greater (but statistically not significant) incidence of thyroid gland adenomas or carcinomas (combined) in dosed male and female mice; (6) a significantly increased incidence in male mice, at both doses, of follicular cell hyperplasia, considered by many as a precursor to thyroid tumors; and (7) an apparent absence of genotoxic potential.

Based on the results of the chronic and genotoxicity studies, NTP (1986) concluded that there was "some evidence of carcinogenicity" for male and female rats as shown by increased incidences of neoplastic nodules of the liver in low-dose males and high-dose groups of each sex. There was "equivocal evidence of carcinogenicity" for male mice as shown by increased incidences of hepatocellular adenomas or carcinomas (combined) in only the low-dose group and slight increase of thyroid gland follicular cell adenomas or carcinomas (combined) in both dosed groups. There was "no evidence of carcinogenicity" for female mice. Several nonneoplastic lesions were observed at increased incidences, the most notable being thyroid gland follicular cell hyperplasia in male mice. The weight of experimental evidence is on the strong end of the spectrum for the descriptor "suggestive evidence of carcinogenic potential," since there is suggestive evidence that decaBDE is carcinogenic for more than one species, sex, and site. Based on the weight of evidence, a dose-response assessment of the carcinogenicity of decaBDE is deemed appropriate

4.6.2. Synthesis of Human, Animal, and Other Supporting Evidence

No information is available on the carcinogenicity of decaBDE in humans. Chronic dietary studies of decaBDE have been conducted in rats and mice (NTP, 1986), and carcinogenicity data are presented in Tables 4-4 and 4-5. DecaBDE caused substantial dose-related increases in neoplastic nodules in rats with statistical significance at the high dose in both sexes (Table 4-4). There were no statistically significant changes in hepatocellular carcinoma in either sex. Although there was a positive trend in mononuclear cell leukemia in male rats, the increase was marginal and not considered to be biologically significant due to the unusually high incidence in controls.

In mice, insignificant increases in hepatocellular adenoma occurred in males at low (3,200 mg/kg-day) and high (6,650 mg/kg-day) doses compared with controls. The incidence of hepatocellular carcinoma was not significantly increased in male mice at either dose. In these male mice, however, significantly increased hepatocellular adenomas or carcinomas (combined) were observed in the low-dose group but only marginally increased in the high-dose group. An increased incidence of hepatocellular adenoma and carcinoma was also observed in the female mice; however, these changes were not statistically significant in either treated dose group. There was also a slight (but not statistically significant) increase in the incidence of thyroid tumors in mice of both sexes, but this was not observed in rats. The biological relevance of this finding in mice is supported by the accompanying increased incidence of follicular cell hyperplasia in male mice; the increase in hyperplasia in females was not statistically significant.

The increased incidence of neoplastic nodules of the liver observed in male and female rats constitutes some evidence of carcinogenicity in treated rats, and this observation is supported by the significantly increased incidence of hepatocellular adenoma and carcinoma (combined) in low-dose male mice and nonsignificantly increased incidence in female mice. Although the study results from each individual species/sex combination were judged to be either "some" or "equivocal" evidence of carcinogenicity, a common target organ (liver) in two species and both sexes indicates a potential for decaBDE to cause cancer in treated animals. In addition to the liver cancer, slight increases in thyroid follicular cell tumors in mice were accompanied by hyperplasia. Based on the increasing agreement that hyperplasia is a stage of the thyroid follicular cell carcinogenic process (NAS, 2000; Hard, 1998; U.S. EPA, 1998b; Hill et al., 1989), decaBDE would be considered as eliciting a carcinogenic effect in a second target organ (i.e., the thyroid) in mice.

4.6.3. Mode-of-Action Information

Genotoxicity studies have found that decaBDE does not appear to be mutagenic since it did not induce gene mutations in *S. typhimurium* strains or in mouse L5178Y lymphoma cells. Also, decaBDE did not induce sister-chromatid exchanges or chromosomal aberrations in

Chinese hamster ovary cells in the presence or absence of metabolic activation systems (NTP, 1986).

There are no other studies of the carcinogenic mode of action of decaBDE. The mode of action is unknown.

Table 4-4. Incidence of liver neoplastic nodules and carcinomas in rats fed decaBDE for 2 years

		Males			Females		
Dose groups	**ppm**	**0**	**25,000**	**50,000**	**0**	**25,000**	**50,000**
	mg/kg-day	**0**	**1,120**	**2,240**	**0**	**1,200**	**2,550**
Number examined		**50**	**50**	**50**	**50**	**50**	**50**
Liver neoplastic nodules							
Overall rates		1/50 (2%)	7/50 (14%)[a]	15/49 (31%)[a]	1/50 (2%)	3/49 (6%)	9/50 (18%)[a]
Adjusted rates		2.9%	27.1%	52.7%	2.5%	9.1%	24.4%
Terminal rates		1/35 (3%)	6/24 (25%)	13/26 (50%)	1/40 (3%)	3/33 (9%)	7/34 (21%)
Week of first observation		104	89	87	104	104	87
Historical incidence			3.5%			2.6%	
Hepatocellular carcinoma							
Overall rates		1/50 (2%)	1/50 (2%)	1/49 (2%)	0/50 (0%)	2/49 (4.1%)	0/50 (0%)
Liver neoplastic nodule or hepatocellular carcinoma							
Overall rates		2/50 (4%)	8/50 (16%)[a]	15/49 (31%)[a]	1/50 (2%)	5/49 (10%)	9/50 (18%)[a]
Adjusted rates		5.2%	31.1%	52.7%	2.5%	15.2%	24.4%
Terminal rates		1/35 (3%)	7/24 (29%)	13/26 (50%)	1/40 (3%)	5/33 (15%)	7/34 (21%)
Week of first observation		97	89	87	104	104	87

[a] Statistically significantly different from controls ($p < 0.05$), based on life table tests and incidental tumor tests.

Source: NTP (1986).

Table 4-5. Incidence of nonneoplastic or neoplastic lesions in the liver and thyroid gland of mice fed decaBDE for 2 years

		Males			Females		
Dose groups	**ppm**	**0**	**25,000**	**50,000**	**0**	**25,000**	**50,000**
	mg/kg-day	**0**	**3,200**	**6,650**	**0**	**3,760**	**7,780**
Number examined		**50**	**50**	**50**	**50**	**50**	**50**
Hepatocellular adenoma							
Overall rates		4/50 (8%)	12/50 (24%)	12/50 (24%)	5/50 (10%)	10/50 (20%)	7/50 (14%)
Adjusted rates		19.0%	46.2%	39.0%	16.8%	31.2%	21.9%
Terminal rates		3/19 (16%)	11/25 (44%)	7/24 (29%)	4/27 (15%)	9/31 (29%)	7/32 (22%)
Week of first observation		81	100	60	83	102	103
Hepatocellular carcinoma							
Overall rates		5/50 (10%)	14/50 (28%)	8/50 (16%)	3/50 (6%)	4/50 (8%)	7/50 (14%)
Adjusted rates		20.7%	42.9%	26.8%	10.7%	12.1%	20.8%
Terminal rates		1/19 (5%)	8/25 (32%)	4/24 (17%)	2/27 (7%)	3/31 (10%)	6/32 (19%)
Week of first observation		81	72	76	101	93	96
Hepatocellular adenoma or carcinoma							
Overall rates		8/50 (16%)	22/50 (44%)[a]	18/50 (36%)	8/50 (16%)	13/50 (26%)	13/50 (26%)
Adjusted rates		33.9%	67.7%	56.5%	26.7%	39.1%	39.1%
Terminal rates		4/19 (21%)	15/25 (60%)	11/24 (46%)	6/27 (22%)	11/31 (35%)	12/32 (38%)
Week of first observation		81	72	60	83	93	96
Thyroid gland							
Hyperplasia, follicular cell		2/50 (4%)	10/50 (20%)[a]	19/50 (38%)[a]	4/50 (8%)	9/50 (18%)	7/49 (14%)
Follicular cell adenoma							
Overall rates		0/50 (0%)	3/50 (6%)	3/50 (6%)	1/50 (2%)	3/50 (6%)	2/49 (4%)
Adjusted rates		0%	10.8%	12.5%	2.9%	7.8%	6.3%
Terminal rates		0/19 (0%)	2/25 (8%)	3/24 (13%)	0/27 (0%)	1/31 (3%)	2/32 (6%)
Week of first observation			90	103	95	80	103
Follicular cell adenoma or carcinoma (combined)							
Overall rates		0/50	4/50 (8%)	3/50 (6%)	1/50 (2%)	3/50 (6%)	3/49 (6%)
Adjusted rates		0%	14.7%	12.5%	2.9%	7.8%	9.4%
Terminal rates		0	3/25 (12%)	3/24 (13%)	0/27 (0%)	1/31 (3%)	3/32 (9%)
Week of first observation			90	103	95	80	103

[a] Statistically significantly different from controls ($p < 0.05$), based on life table tests and incidental tumor tests.

Source: NTP (1986).

4.7. SUSCEPTIBLE POPULATIONS AND LIFE STAGES

4.7.1. Possible Childhood Susceptibility

As discussed in section 4.3.1, a gavage study (Hardy et al., 2002) in which rats were exposed in the diet to decaBDE (97.34% purity) during gestation days 0–19 reported no effects on number of dams with viable fetuses, mean number of corpora lutea, number of implantation sites, percent preimplantation loss per dam, number of viable fetuses, gravid uterine weights, fetal body weights, crown-rump ratio, and fetal sex ratio. No effects were reported during external, skeletal, or visceral examination of rat fetuses. The NOAEL in this study was 1,000 mg/kg-day, the highest dose tested. In a study in male mice (Tseng et al., 2006) exposed to BDE-209 from PNDs 21–70 (see section 4.3.2), effects were seen on sperm function, DNA content, and histopathology of the testes at 500 mg/kg-day but not at 100 mg/kg-day.

In a study in rats (Viberg et al., 2007), exposure of the animals to the lowest dose tested of 6.7 mg/kg-day BDE-209 on PND 3 resulted in significant changes in spontaneous motor behavior (locomotion, rearing, and total activity) in 2-month-old rats. In the study of Rice et al. (2007), effects on the palpebral reflex, struggling behavior and locomotor activity were seen in mice given the lowest dose of 6 mg/kg-day BDE-209 on PNDs 2–15.

Neurobehavioral alterations were observed in mature mice when male mice were exposed to 20.1 mg/kg decaBDE as neonates on PND 3 but not on PNDs 10 and 19 (Viberg et al., 2003a). A significant increase in the amount of radioactivity in the brain on day 7 after exposure was noted when the neonates were exposed to ^{14}C-decaBDE on PNDs 3 and 10 but not on PND 19 (Viberg et al., 2003a). The increase in the radioactivity in the brain, coupled with the behavioral disturbances on exposure to decaBDE on PND 3, suggests that differences may exist in the absorption and distribution of decaBDE among the 3-, 10-, and 19-day-old neonates. In addition, differences exist in the timing of the brain growth spurt in rodents (first few weeks after birth) and humans (starts in the sixth month of gestation and continues through the first 2 years of life after birth). The significance of this difference with regard to the potential for effects on children from exposure to BDE-209 is not clear. Moreover, whether other targets of decaBDE (thyroid and liver) are more sensitive in children is unknown since the enzymes responsible for decaBDE metabolism have not been identified and the mechanisms for age-dependent kinetic differences are not completely clear. Although no studies were identified that investigated placental transfer, decaBDE has been found in human breast milk, suggesting that newborns and infants have a potential source of exposure via this route.

4.7.2. Possible Gender Differences

All absorption studies following oral administration of decaBDE were conducted in male rats, precluding a comparison of kinetics in males versus females. There were no clear gender-dependent differences in decaBDE toxicity in short-term and subchronic studies conducted in both sexes of rats and mice (NTP, 1986). However, long-term exposure studies to decaBDE indicated that male rats may be more sensitive than females. Male rats exhibited nonneoplastic lesions, including liver thrombosis and degeneration, splenic fibrosis, and lymphoid hyperplasia, and male mice showed increased incidences of liver granulomas, hepatocellular hypertrophy, and thyroid follicular cell hyperplasia, while female rats and mice appeared to be refractory to these systemic effects of decaBDE at the tested doses (NTP, 1986). One exception was that female mice had a higher incidence of stomach ulcers than their male counterparts. Although a significantly increased incidence of liver neoplastic nodules was observed in both sexes of rats (NTP, 1986), hepatocellular carcinomas or adenomas were not significantly increased in male mice only. No gender-specific effects on reproductive organs were identified.

The study of Rice et al. (2007) investigated several endpoints in male and female mice. In PND 21 offspring of mice treated with decaBDE on PNDs 2–15, a dose-related reduction in serum T_4 was observed in males but not females. Development of forelimb grip strength was delayed at PND 16 in exposed males in the high-dose group but not in females. Struggling behavior was more apparent in males than in females, and effects on locomotor activity were observed on PND 70 in male mice but not in female mice.

Overall, it appears that males may be more susceptible to some effects of decaBDE compared to females, although this is not true for all endpoints. Underlying mechanisms for the apparent differences in susceptibility have not been identified.

5. DOSE-RESPONSE ASSESSMENTS

5.1. ORAL REFERENCE DOSE (RfD)

5.1.1. Choice of Principal Study and Critical Effect—with Rationale and Justification

Epidemiological studies or case reports are not available for decaBDE.

Available animal studies of repeated oral exposure to decaBDE include a 4-day study in rats (Zhou et al., 2001), 14-day studies in rats and mice (NTP, 1986), 13-week studies in rats and mice (NTP, 1986), and 2-year studies in rats and mice (NTP, 1986). In addition, decaBDE was also tested for its toxicity in reproductive and developmental studies (Rice et al., 2007; Viberg et al., 2007, 2003a; Tseng et al., 2006; Hardy et al., 2002). The results from these studies are summarized in Tables 4-1, 4-2, and 4-3. Among the available studies, several potential principal studies for deriving an RfD were identified: the 2-year chronic studies in rats and mice (NTP, 1986) and neurodevelopmental studies in rats and mice (Rice et al., 2007; Viberg et al., 2007, 2003a).

NTP (1986) reported a study of the chronic oral toxicity and carcinogenicity of decaBDE in rats. In the liver, an increase in the incidence of thrombosis was observed in high-dose male rats (2,240 mg/kg-day). A dose-dependent but statistically not significant increase in degeneration of the liver was also observed in treated male rats at incidences of 13/50, 19/50, and 22/49 in the control, low-dose, and high-dose groups, respectively. In the spleen, increased incidence of fibrosis was seen in males at the low dose (8/50) and high dose (13/49) compared tc 5/49 in controls; the effect was statistically significant only in the high-dose group. In the mandibular lymph node, lymphoid hyperplasia increased in males in a dose-dependent manner, but the incidence reached statistical significance only at the high dose. Based on these results, the NOAEL for systemic toxicity was 1,120 mg/kg-day, and the LOAEL was 2,240 mg/kg-day in male rats based on increased incidence of thrombosis and degeneration in the liver, splenic fibrosis, and lymphoid hyperplasia of the mandibular lymph nodes. Female rats appeared to be refractory to the systemic toxicity of decaBDE at the doses used in this study. Therefore, the NOAEL for systemic toxicity in females was 2,550 mg/kg-day, with no LOAEL established.

The observed systemic toxicity of decaBDE in the 2-year study in rats is supported by observed liver effects at higher doses in a 2-year study in mice (NTP, 1986). Significant increases in the incidence of centrilobular hypertrophy were also observed in the liver of male mice at low and high doses (34/50, and 32/50, respectively) in comparison to controls (0/50). In the thyroid gland, a dose-dependent and statistically significant increase (at both dose levels) in the incidence of follicular cell hyperplasia was observed in male mice (control, 2/50; low dose, 10/50; high dose, 19/50). In the females, this incidence increased in the low- and high-dose groups compared with the control group, but the increase was not dose dependent or statistically significant at any dose level. High-dose female mice exhibited a significant increase in the incidence of stomach ulcers. Based on these results, no NOAEL for males was established. The LOAEL, based on increased incidence of centrilobular hypertrophy and a statistically significant and dose-dependent increase in thyroid gland follicular cell hyperplasia in male mice, was 3,200 mg/kg-day or greater. Similar to the study in rats (NTP, 1986), female mice appeared to be refractory to the systemic toxicity of decaBDE at the doses used in this study. The study established a NOAEL of 3,760 mg/kg-day for portal-of-entry effects for females and a LOAEL of 7,780 mg/kg-day based on a significant increase in the incidence of stomach ulcers.

Viberg et al. (2003a) reported functional neurobehavioral effects of single-dose exposures to decaBDE. The neurotoxic effects of decaBDE on spontaneous motor behavior were investigated in adult NMRI male mice exposed to a single oral dose of decaBDE as neonates on PND 3, 10, or 19 (i.e., at different stages of neonatal mouse brain development). Pair-wise testing between adult mice exposed on PND 3 and control groups indicated significant dose-related changes in the habituation ratio calculated from three behavior variables (locomotion, rearing, and total activity) in mice exposed to 20.1 mg/kg and evaluated at 2, 4, and 6 months of age; no statistically significant effect was seen at 2.22 mg/kg. Adult mice exposed neonatally up to 20.1 mg/kg on either PND 10 or 19 did not show any significant differences in any of the variables after 2, 4, or 6 months compared with controls. The authors indicated that the absence of changes in spontaneous activity in mice treated on PNDs 10 and 19 appears to suggest that there is a critical window for the induction of behavioral disturbances. The decrease observed in the habituation capability in the adult mice exposed neonatally to the high dose indicated that the neurotoxic effect of neonatal decaBDE exposure was persistent and also worsened with age. Based on these observations, the NOAEL in this study was 2.22 mg/kg and the LOAEL was 20.1 mg/kg. In the study in rats (Viberg et al., 2007), significant dose-related disruption in habituation (changes in locomotion, rearing, and total activity) was observed in 2-month-old rats, following exposure to BDE-209 at 6.7 and 20.1 mg/kg on PND 3. A NOAEL was not identified in this study.

Rice et al. (2007) examined the effects of BDE-209 (99.5% purity) on developmental milestones, sensorimotor behaviors, serum T_4 levels and locomotor activity in male and female C57BL6/J mice administered doses of 0, 6, or 20 mg/kg-day from PNDs 2–15. An FOB suitable for neonatal mice was developed to examine a series of homecage, reflexive, and sensorimotor behaviors, measured on PND 14, 16, 18, or 20. Three of the FOB endpoints were affected by BDE-209 exposure: palpebral reflex, forelimb grip, and struggling behavior during handling. On PND 14, significantly fewer male and female pups in the 6 and 20 mg/kg-day groups performed the palpebral reflex compared with controls. On PNDs 14 and 16, fewer male pups in the 20 mg/kg-day group performed an effective forelimb grip compared with same-sex controls. Male and female pups in the 6 mg/kg-day group struggled significantly more on PND 20, while they were being handled for the FOB, compared with controls and the high-dose group. Locomotor activity in PND 70 males and females in the control and treated groups declined over the course of the 2-hour assessment. However, the rate of decline was significantly different ($p = 0.04$) in male mice exposed to 6 and 20 mg/kg-day compared with control animals. The effect was most pronounced in the high-dose males during the first 1.5 hours of the 2-hour activity session. A dose-related reduction in serum T_4 in comparison with controls occurred in PND 21 males but not in females. The LOAEL in this study was 6 mg/kg-day, the lowest dose tested, for decrease in the percent of male and female pups performing the palpebral reflex on PND 14, for increased struggling behavior of male mice on PND 20, for decreased T_4 levels in male mice, and for effects on locomotor activity of male mice on PND 70.

Viberg et al. (2007) administered BDE-209 by gavage to 3-day-old Sprague-Dawley rats at 0, 6.7, or 20.1 mg/kg. A total of 20 rats were picked from three to five different litters in each treatment group. Motor activity, measured as locomotion (horizontal movement), rearing (vertical movement), and total activity (all types of vibration within the test cage [i.e., those caused by rat movements, shaking/tremors, and grooming]) was evaluated for a 60-minute period, divided into three 20-minute periods, in rats at the age of 2 months. In control rats, there was a distinct decrease in locomotion, rearing, and total activity, indicating habituation in response to the diminishing novelty of the test chamber over the 60-minute test period, at 2 months of age. Two-month-old rats exposed to 20.1 mg/kg BDE-209 on PND 3 displayed significantly less activity for all three behavioral variables during the first 20-minute test period compared with controls, while during the third 20-minute period (40–60 minutes) they were significantly more active than the control animals. Rats receiving the low dose of BDE-209 (6.7 mg/kg) showed significantly increased locomotion activity during the second 20-minute period, significantly decreased rearing activity during the first and second 20-minute periods, and significantly higher total activity during the first and second 20-minute periods compared with the control rats. The LOAEL in this study was 6.7 mg/kg for significant changes in spontaneous motor behavior (locomotion, rearing, and total activity) in 2-month-old rats given BDE-209 on PND 3.

Of the three neurobehavioral studies, only Viberg et al. (2003a) identified a NOAEL. The NOAEL identified in Viberg et al. (2003a) was lower than the LOAELs identified in the neurobehavioral studies conducted by Viberg et al. (2007) and Rice et al. (2007). The Viberg et al. (2003a) study was therefore selected as the principal study for deriving the RfD. However, several considerations were weighed in making this decision. Concerns regarding the study design raise potential issues about full reliance on this study. The dosing regimen did not include gestation and lactation exposure (U.S. EPA, 1998a); only single doses were given. The study was conducted in male mice only. The protocol was unique and did not conform to health effects test guidelines for neurotoxicity screening battery or developmental neurotoxicity studies

(U.S. EPA, 1998a, c). While the study design appears to identify a developmental window of susceptibility, it is not adequate to determine the effect of longer dosing. However, the fact that the effects were observed after a single dose is a situation that increases concern regarding the impact of BDE-209 on neurological development. Translating the implications of these data to more traditional dosing regimens is problematic, particularly with regard to evaluating the implications of in utero and postnatal exposure.

Another concern is that, based on the data provided in the published report, more than one pup per litter were used for the behavioral testing (10 mice were randomly selected from three to five different litters in each treatment group). Increasing the number of samples from each litter may bias the analyses towards false positives. The observed neurobehavioral effects may be attributable to differences in pups born to a single dam rather than related to treatment. Another concern regarding the study design was the limited number of neurobehavioral parameters that were assessed; the authors measured only indices related to motor activity (locomotion, rearing, and total activity). The absence of a full FOB that evaluates neurological and behavioral signs limits the ability to correlate the reported effects with other FOB parameters. Data from the FOB utilized in the Rice et al. (2007) study, also in mice, mitigate some concern related to its absence in the Viberg et al. (2003a) study.

As indicated in the *Guidelines for Neurotoxicity Risk Assessment* (U.S. EPA, 1998a), it is assumed that an agent that produces detectable adverse neurotoxic effects in experimental animal studies will pose a potential hazard to humans. For BDE-209, in the absence of human evidence, data from experimental animal studies are used as the basis for the RfD.

While study design limitations cloud the utility of this study, several additional considerations support the use of these data. Acute exposure to a highly lipophilic and long half-life chemical, such as BDE-209, will result in exposure that lasts much longer than just acutely. In addition, there are a wide variety of brain structures that have very limited critical windows during development. These short critical windows translate to susceptible periods of exposure that can be very short.

The concept that exposure during critical periods of development can induce functional neurological effects later in development has been demonstrated with structurally related PBDE congeners, including tetra-, penta-, and hexaBDEs (Kuriyama et al., 2005; Viberg et al., 2005, 2004a, b, 2003b, 2002; Ankarberg, 2003; Branchi et al., 2002; Eriksson et al., 2002, 2001). In addition, the study of Rice et al. (2007) strengthens the evidence that links the behavioral effects seen in mice to neonatal BDE-209 exposure. Therefore, the observed neurobehavioral effects in the Viberg et al. (2003a) study in mice and the Viberg et al. (2007) study in rats are biologically plausible, and exposure to BDE-209 may pose a potential hazard to humans (U.S. EPA, 1998a).

Viberg et al. (2003b) have suggested that the animals are vulnerable only during the postnatal brain growth spurt that occurs in the first few weeks after birth in mice. In the case of decaBDE, the identification of PND 3 as the most vulnerable window for exposure can be explained by the toxicokinetic data showing apparent absorption decreases during the first few weeks of life and slow distribution to the brain when the dosing occurs on PND 3 or 10. Although some radiolabel reaches the brain in the 24 hours after dosing, the amount increases over the 7-day period after dosing. After dosing on PND 19, less than 0.1% of the dose was found in the brain initially and after 7 days. These observations would explain the absence of effects in animals exposed later in the postnatal period as adults.

Taken together, these considerations support the use of the Viberg et al. (2003a) study as a potential critical study for deriving the RfD for BDE-209.

5.1.2. Methods of Analysis

The published information presented by Viberg et al. (2007, 2003a) could not be used for benchmark dose (BMD) modeling; mean values for motor activity (locomotion, rearing, and total activity), habituation capability for 2-, 4-, and 6-month-old mice or rats, and standard deviations are only displayed graphically, and such values cannot be read with any accuracy from the graphs. Therefore, the NOAEL of 2.22 mg/kg is used as a point of departure for estimating the oral RfD for BDE-209.

DecaBDE has very low water solubility and a relatively high K_{ow}; therefore, preferential distribution to adipose tissue might be expected. This property raises concerns for accumulation of decaBDE in the body as a result of repeated exposure. However, limited data on the tissue distribution of decaBDE in experimental animals indicate that it is not readily distributed to adipose tissue (Morck et al., 2003). The limited deposition in the adipose tissue suggests that chronic accumulation may not be significant for BDE-209. The optimal way to address this issue would be to use a PBPK model to estimate the steady-state body burden in the lipid compartment after repeated exposure and examine the dose-response relationship based on the internal dose at the target tissues. No PBPK models of decaBDE were identified for humans or animals, and data on internal doses from existing toxicity studies are not adequate to support dose-response analysis. In the absence of these data, a dose-response analysis based on body burden was not included in this assessment.

5.1.2.1. *Benchmark Dose Modeling*

Although the NOAEL from the Viberg et al. (2003a) study was selected as the critical endpoint for the RfD derivation, the dose-response data from the NTP (1986) study were modeled to determine the lower bound BMD (BMDL) for systemic toxicity. Details of the BMD modeling results are presented in Appendix B and summarized in this section. The following data sets from the NTP (1986) 2-year rat and mouse studies were selected for BMD modeling: thrombosis in the liver, liver degeneration, fibrosis in the spleen, and lymphoid hyperplasia in male rats; centrilobular hypertrophy in the livers; and follicular cell hyperplasia in the thyroid of male mice.

The BMD modeling was conducted using EPA's BMD software (BMDS) version 1.3.2. The dose levels showing a change compared with control values exhibited responses at levels near 10%; therefore, all of the BMD analyses were conducted with the benchmark response (BMR) set to a 10% extra risk (U.S. EPA, 2000b). For each data set, all the dichotomous models, including gamma, logistic, log-logistic, multistage, probit, log-probit, quantal-linear, quantal-quadratic, and Weibull, available in the BMDS were used. BMD model fit was evaluated based on the goodness-of-fit *p* value (indicating global model fit), Akaike Information Criterion (AIC) (indicating model fit when controlling for number of model parameters), as well as local chi-square residual (indicating the model fit at the data point close to the preset BMR). Based on the model output, the models providing best model fit to the data were selected to estimate BMD$_{10}$ and BMDL$_{10}$. The BMD analyses results are summarized in Table 5-1.

Based on the comparison of BMD modeling results for all the potential critical effects observed in chronic rat and mouse studies, the lowest BMDL$_{10}$ is 406 mg/kg-day for liver degeneration effect in male rats. This value is much higher than the NOAEL of 2.22 mg/kg for the neurobehavioral changes observed in Viberg et al. (2003a). Because the graphic habituation data from the Viberg et al. (2003a) publication could not be used for BMD modeling, the NOAEL of 2.22 mg/kg is used as a point of departure for calculating the oral RfD.

Table 5-1. BMDs for potential critical effect from chronic rat and mouse studies

Endpoint	Reference	NOAEL (mg/kg-day)	LOAEL (mg/kg-day)	BMD$_{10}$ (mg/kg-day)	BMDL$_{10}$ (mg/kg-day)
Thrombosis in the liver of male rats	NTP (1986)	1,120	2,240	2,125	1,738
Liver degeneration in male rats	NTP (1986)	2,240	N/A[a]	765	406
Splenic fibrosis in male rats	NTP (1986)	1,120	2,240	1,446	1,001
Lymphoid hyperplasia in male rats	NTP (1986)	1,120	2,240	1,538	1,165
Centrilobular hypertrophy in the liver of male mice	NTP (1986)	N/A	3,200	No model fit	–
Follicular cell hyperplasia in the thyroid of male mice	NTP (1986)	N/A	3,200	1,670	1,190

[a]N/A = not available or cannot be estimated.

Source: NTP (1986).

5.1.3. RfD Derivation

Based on the neurobehavioral effects observed in the Viberg et al. (2003a) study, the NOAEL of 2.22 mg/kg is used as the point of departure for calculating the RfD. The following uncertainty factors (UFs) (U.S. EPA, 2002) are applied to the NOAEL of 2.22 mg/kg: 10 for extrapolating animal data to humans (UF_A interspecies variability), 10 for susceptible human subpopulation (UF_H interhuman variability), and 3 for extrapolating from the single-dose to a lifetime exposure (UF_S). The total composite $\mathrm{UF} = 10 \times 10 \times 3 = 300$.

A 10-fold UF_A was used to account for laboratory animal to human interspecies differences. Although the toxicokinetics of decaBDE in animals have been evaluated, no adequate description of toxicokinetics of decaBDE in humans exists. The critical effect for deriving the RfD, altered behavior due to exposure during development, is expected to be relevant to humans. No quantitative data were identified to compare relative human and rodent sensitivity to these changes. However, given the longer period of brain development in humans as compared to rodents and the higher importance of cognitive function, it is appropriate to consider that humans may be more sensitive than rodents in the absence of specific data. Based on these considerations, the default UF_A value of 10 was applied.

A default intraspecies UF_H of 10 was applied to account for variations in susceptibility within the human population (intrahuman variability). This factor accounts for the segment of the human population that may be more sensitive than the general population to exposure to BDE-209. A default value is warranted because insufficient information is currently available to assess human-to-human variability in BDE-209 toxicokinetics or toxicodynamics.

A threefold UF_S was used to adjust for exposure duration. For BDE-209, the principal study identified endpoints that, for the most part, reflect specific aspects of developmental physiology. The hypothesized window of susceptibility, proposed by the study authors, is based on the observation that the developmental neurotoxic effects observed following exposure to BDE-209 on PND 3 will not occur once the toxicokinetics of intestinal uptake and excretion have matured and the animal brain is developmentally less active (outside the window of susceptibility). The Eriksson/Viberg group has suggested that the period of maximum vulnerability for the developing cholinergic system that coincides with the most pronounced neurodevelopmental effects from BDE-99 exposure is from PNDs 10–14. However, for BDE-209 the developmental neurotoxic effects were noted following exposure on PND 3 rather than on PNDs 10 or 19. It is likely that two factors contributed to this difference in the timing for the peak period of vulnerability. First, absorption from the gastrointestinal tract decreases as the neonatal mice age during their first few weeks of life; thus, less of the BDE-209 reaches the liver for distribution on PNDs 10 and 19 than on PND 3. Secondly, distribution to the brain is slow. The amount of radiolabel in the brain is 1.4- and 2.8-fold greater 7 days after dosing compared with 24 hours after dosing on PNDs 3 and 10. Even less reaches the brain when the BDE-209 is administered on day 19. The UF_S was viewed as a dosing duration adjustment rather than simply a comparison of the effects of a subchronic to a chronic exposure. A threefold UF_S was applied because the critical study dosed the animals only once within the hypothesized critical window, not because the chronic exposures would have exacerbated the impact on habituation.

A UF_L for LOAEL-to-NOAEL extrapolation was not applied because a NOAEL was used as the point of departure.

A UF_D to account for deficiencies in the available decaBDE database was not necessary. Available animal studies on repeated oral exposure to decaBDE include 14-day studies in rats and mice (NTP, 1986), 13-week studies in rats and mice (NTP, 1986), and 2-year studies in rats and mice (NTP, 1986). A developmental and behavioral toxicity study in male and female mice was available (Rice et al., 2007), as well as a behavioral study in male rats (Viberg et al., 2007). A 7-week study (Tseng et al., 2006) of sperm functions in mice was also available. In addition, a standard developmental toxicity study in rats (Hardy et al., 2002) was identified for decaBDE. No multigeneration reproductive toxicity study or other study of reproductive function is available for pure decaBDE. This array of studies results in potential uncertainty regarding the reproductive toxicity of decaBDE. However, this potential uncertainty is adequately accounted for based on the following considerations. First, none of the well-conducted longer-term dosing studies identified effects on male or female reproductive organs. Second, no developmental or reproductive effects were observed at doses up to 1,000 mg/kg-day in rats (Hardy et al., 2002) and 100 mg/kg-day in mice (Tseng et al., 2006). The absence of effects in the available longer-term and developmental studies indicates that at least some aspects of reproductive organ toxicity or function are not affected at doses much higher than those that resulted in the neurological effects in neonates (Viberg et al., 2003a), although effects on mating and fertility are not evaluated in these studies.

The other potential uncertainty in the database factor is immunotoxicity from exposure to decaBDE. The potential immunotoxicity was indicated by the observations of significant increases in spleen fibrosis and lymphoid hyperplasia in male rats treated with a high dose of decaBDE (NTP, 1986). However, no such changes occurred in female rats or in either sex of treated mice (NTP, 1986). In addition, an in vitro immunotoxicity study (Pullen et al., 2003) with mouse splenocytes suggested that decaBDE is not likely to affect the immune system in an immunosuppressive manner nor the production of the cytokines by these cells. Moreover, the proposed point of departure is based on the developmental neurobehavioral changes and immunotoxicity is not likely to occur at the current point of departure of 2.22 mg/kg, which is 500-fold lower than the NOAEL for histopathologic changes in rat spleen and lymphoid in the NTP (1986) study.

Based on the choice of the critical effect and UF selections, the oral RfD for decaBDE is calculated as follows:

$$\begin{aligned} \text{RfD} &= \text{NOAEL} \div \text{UF} \\ &= 2.22 \text{ mg/kg} \div 300 \\ &= 0.007 \text{ mg/kg-day or } 7\ \mu\text{g/kg-day} \end{aligned}$$

5.1.4. Previous RfD Assessment

An IRIS health assessment of decaBDE is available (U.S. EPA, 1989). The RfD is based on the study of Kociba et al. (1975) in which male and female Sprague-Dawley rats (25/sex/dose group) were treated with a commercial decaBDE (77.4% decabromodiphenyl oxide, 21.8% nonaBDE, and 0.8% octaBDE) at doses of 0, 0.01, 0.1, or 1.0 mg/kg-day for 2 years. Parameters examined were hematology, clinical chemistry, food consumption, organ weight, body weight, and incidence of histopathologic lesions. No significant differences among treatment and control groups were found. The NOAEL in this study was 1.0 mg/kg-day, the highest dose tested. A UF of 100 was applied to the NOAEL for both the expected intra- and interspecies variability to the toxicity of this chemical in lieu of specific data, resulting in a RfD of 0.01 mg/kg-day or 10 µg/kg-day. Confidence in the RfD was considered low (The low doses and number of animals used in this study have been questioned as to their adequacy to determine the carcinogenic potential of this commercial decaBDE [NTP, 1986]). The previous RfD was not based on the NTP (1986) study because the final NTP report was not available at the time.

The National Research Council of the National Academies of Science (NAS, 2000) derived a RfD for decaBDE based on the NTP (1986) study. The LOAEL for liver thrombosis and degeneration in male rats was 2240 mg/kg-day and the NOAEL 1120 mg/kg-day. The following UFs were applied: 10 for extrapolation from animals to humans, 10 for intraspecies variation, and 3 for database deficiency. Applying this total UF of 300 to the NOAEL of 1120 mg/kg-day gives a RfD of 4.0 mg/kg-day. Confidence in this provisional RfD was considered medium to low.

The Agency for Toxic Substances and Disease Registry (ATSDR, 2004) derived an intermediate oral minimal risk level (MRL) of 10 mg/kg-day based on the Hardy et al. (2002) study. No effects on any maternal or fetal endpoints were observed in any dose group. The NOAEL in this study was the highest dose tested of 1000 mg/kg-day. Applying a total UF of 100 (10 for extrapolation from animals to humans and 10 for human variability), an intermediate oral MRL of 10 mg/kg-day was derived.

5.2. INHALATION REFERENCE CONCENTRATION (RfC)

No data are available for deriving a RfC for decaBDE.

5.3. CANCER ASSESSMENT

5.3.1. Choice of Study/Data—with Rationale and Justification

As discussed in section 4.6, the weight of evidence of human carcinogenicity of decaBDE is based on (1) no studies of cancer in humans exposed to decaBDE; (2) a significantly increased incidence of neoplastic nodules in the liver of low- and high-dose male rats and high-dose female rats; (3) a significantly increased incidence of hepatocellular adenoma or carcinoma (combined) in male mice at low dose and marginally increased incidence at high dose; (4) a nonsignificantly increased incidence of hepatocellular adenoma or carcinoma (combined) in female mice; (5) a slight (but statistically not significant) increase in incidence of thyroid gland adenomas or carcinomas (combined) in both male and female mice; (6) a significantly increased incidence in male mice of follicular cell hyperplasia, considered by many as a precursor to thyroid tumors; and (7) an apparent absence of genotoxic potential. All of the data supporting carcinogenicity were obtained from chronic studies in rats and mice (NTP, 1986).

As discussed in section 4.6, the weight of evidence suggests that decaBDE shows "suggestive evidence of carcinogenic potential." Support for tumorigenic effects in the liver of varying strengths is found in both sexes of rats and mice. In the NTP (1986) study, decaBDE caused a dose-dependent increased incidence of liver neoplastic nodules in rats with statistical significance at the high dose in both sexes (Table 4-4), indicating some evidence of carcinogenicity in treated rats. However, there were no significant changes in hepatocellular carcinoma in either sex. In mice, nonsignificant increases in hepatocellular adenoma or carcinoma occurred in male mice at low (3,200 mg/kg-day) and high (6,650 mg/kg-day) doses compared with controls. However, combined incidence of hepatocellular adenoma or carcinoma increased significantly in the low-dose group but not in the high-dose group. Increased incidence of hepatocellular adenoma and carcinoma was also observed in the female mice; however, these changes were not statistically significant. Similarly, although the increases in thyroid tumors were not statistically significant in either sex of mice, they were supported by increases in a precursor to thyroid tumors, follicular cell hyperplasia.

Therefore, the NTP (1986) chronic studies in mice and rats were considered the basis for the quantitative cancer assessment. Liver and thyroid tumors were considered as possible bases for the quantitation. To select the most sensitive cancer endpoint as the point of departure to derive a cancer risk value, benchmark modeling was conducted for each tumor endpoint or related precursor (i.e., thyroid hyperplasia). The BMD analysis and corresponding results are summarized in the following sections.

5.3.2. Dose Adjustments

For the chronic rat study (NTP, 1986), the original oral doses were reported as 0, 1,120, and 2,240 mg/kg-day for males and 0, 1,200, and 2,550 mg/kg-day for females. Since there are not enough toxicokinetic data for conducting a quantitative interspecies extrapolation, a default dose conversion was used. Based on EPA's *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a), corresponding human equivalent doses (HEDs) were calculated by scaling animal daily applied doses experienced for a lifetime in proportion to body weight raised to the 0.75 power.

A body weight $(bw)^{3/4}$ scaling factor was used to convert the points of departure in the rat study to HEDs, in accordance with the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a). This procedure presumes that equal doses in these units (i.e., in mg/kg$^{3/4}$-day), when administered daily over a lifetime, will result in equal lifetime risks of the critical effect across mammalian species (U.S. EPA, 1992). The HED may be calculated as follows (U.S. EPA, 2005a, 1992):

$$\text{HED (mg/kg-day)} = \text{dose in animals (mg/kg-day)} \times (bw_a/bw_h)^{0.25}$$

where:

HED = human equivalent dose
dose = average daily dose in animal study
bw_a = animal body weight (kg)
bw_h = reference human body weight (70 kg)

Based on reported weekly body weight data for each dose group for male rats, average lifetime body weights were calculated as 383.9, 385.2, and 380.7 g for the control, low-, and high-dose groups, respectively. Using the calculated average lifetime rat body weight and a default human body weight of 70 kg, the corresponding HEDs were calculated as 0, 305.1, and 608.3 mg/kg-day, respectively. Similarly, for female rats, average lifetime body weights were ~~calculated as 247.9, 246.2,~~ and 242.1 ~~g for the control, low-, and high-dose groups, respectively.~~ Based on the calculated body weight and default human body weight of 70 kg, corresponding HEDs were calculated as 0, 292.2, and 618.4 mg/kg-day, respectively.

For the chronic mouse study (NTP, 1986), the only dose-response data on carcinogenicity available were obtained from male mice; therefore, the dose conversion was conducted for male mice only. The original oral doses for male mice were reported as 0, 3,200, and 6,650 mg/kg-day. Since there are not enough toxicokinetic data for conducting a quantitative interspecies extrapolation, a default dose conversion was used. Based on reported weekly body weight data for each dose group, average lifetime body weights were calculated as 37.3, 37.4, and 37.0 g for control, low-, and high-dose groups, respectively. Based on these data on average lifetime mouse body weight and a default human body weight of 70 kg, corresponding HEDs were calculated by scaling animal daily applied doses experienced for a lifetime in proportion to body weight raised to the 0.75 power. The estimated HEDs are 0, 486.5, and 1,008.6 mg/kg-day, respectively.

5.3.3. Extrapolation Method(s)

U.S. EPA BMDS (version 1.40b) was used in the cancer endpoint BMD analysis. Following the guidelines for evaluation of data on tumorigenic responses, the cancer model (a multistage model with a calculation function for slope factor) was used to calculate effective doses (EDs) for a tumor response within the range of observation and the lower confidence estimate on that dose. The lower confidence limit of the estimated dose for a BMR similar to the response observed in the low-dose group is used as a point of departure to estimate an oral slope factor (U.S. EPA, 2005a, b).

All potential tumor endpoints with statistically significant responses in the rat and mouse chronic studies (NTP, 1986) were modeled in order to identify the most sensitive point of departure. Animals dying prior to week 53, before the first appearance of tumors, were censored from the group totals to adjust the incidence rates for early mortality. To adjust for differential mortality among treated male rats, censored data on neoplastic nodules or the combined neoplastic nodules and carcinomas in rats of both sexes were also modeled. The data on combined hepatic carcinomas and adenomas in male mice were modeled despite the fact that they did not show a good dose-response relationship because they were significantly increased in comparison with controls. A detailed description of the BMD modeling results is presented in Appendix C. The estimated cancer slope factors based on estimated EDs and their 95% lower confidence limits using the multistage model for each cancer endpoint are summarized in Table 5-2.

Table 5-2. Cancer slope factors derived from BMDs for neoplastic effect from chronic rat and mouse studies using the multistage model

Endpoint	Species	Cancer slope factor $(mg/kg\text{-}day)^{-1}$
Neoplastic nodules in the liver	Male rat	0.0007
Neoplastic nodules or carcinomas (combined) in the liver	Male rat	0.0007
Neoplastic nodules in the liver	Female rat	0.0004
Neoplastic nodules or carcinomas (combined) in the liver	Female rat	0.0005
Follicular cell hyperplasia in the thyroid	Male mouse	0.0005
Adenomas or carcinomas (combined) in the liver	Male mouse	0.0005

Source: NTP (1986).

Neoplastic nodules and carcinomas were also modeled together because the two lesions could have a similar mode of action. Based on the estimated ED for each cancer endpoint, the most sensitive response is neoplastic nodule or carcinoma (combined) in the liver of male rats. The ED_{12} from the lower end of the range of observation is 263 mg/kg-day, and the corresponding 95% lower confidence limit for the effective dose (LED_{12}) is 178 mg/kg-day. For neoplastic nodules or carcinomas in the liver of female rats, both censored and uncensored data resulted in higher LEDs than for this effect in male rats; therefore, the LED in females was not used as the point of departure. Similarly, the estimated LED for the follicular cell hyperplasia in the thyroid of male mice is also higher than that of neoplastic nodules or carcinomas (combined) in the male rats. Thus, the lowest LED, 178 mg/kg-day for neoplastic nodules or carcinomas (combined) in the male rats, is selected as the point of departure for deriving an oral cancer slope factor. However, as stated earlier (section 4.2.2.1), the term neoplastic nodule is no longer used for rat liver tumors, and it is not possible to know if all lesions originally categorized as neoplastic nodules were preneoplastic under current guidelines. Some may have been nonneoplastic hyperplasia. Accordingly, there is some uncertainty in the calculated slope factor that should be considered when it is applied in quantitative risk assessment.

5.3.4. Oral Slope Factor

Although no human studies were available, two chronic rodent studies provide suggestive evidence of decaBDE-induced carcinogenicity. The data from these studies are adequate to support a quantitative cancer dose-response assessment. Even though the available evidence is suggestive of human carcinogenic potential, there is very limited information exploring the mode of action for any of the tumors reported in the animal chronic studies. While decaBDE was not mutagenic or genotoxic in various in vitro studies, there are no data to support alternative mode-of-action hypotheses. In the absence of such data, a mode of action for BDE-209 could not be determined; therefore, extrapolation from the point of departure to lower doses is conducted by using a linear approach.

Based on a comparison of estimated EDs for all the cancer endpoints observed in rat and mouse chronic studies (NTP, 1986), the neoplastic nodules or carcinomas (combined) in the liver of treated male rats are the most sensitive endpoint. Therefore, the LED_{12} of 178 mg/kg-day estimated for this endpoint is used as a point of departure for calculating the cancer slope factor.

For linear extrapolation, a straight line is drawn from the point of departure expressed as an HED to the origin to give a probability of extra risk. The slope of the line expresses extra risk per dose unit. For linear extrapolation, the slope of the line is $0.12/LED_{12}$. The central estimate, ED_{12}, of exposure at 12% extra risk is $0.12/ED_{12}$. The slope of the linear extrapolation from the central estimate ED_{12} is 5×10^{-4}, which is derived using 0.12/(263 mg/kg-day). For neoplastic nodules or carcinomas, the resulting oral cancer slope factor is 7×10^{-4} per mg/kg-day, which is derived using 0.12/(178 mg/kg-day). Since some of the neoplastic nodules might not progress to carcinomas, this oral risk estimate errs on the conservative side. Based on this slope factor, the dose associated with an excess cancer risk (risk-specific dose [RSD]) value is approximately as follows: RSD at 10^{-6} is 1 µg/kg-day; RSD at 10^{-5} is 10 µg/kg-day; and RSD at 10^{-4} is 100 µg/kg-day.

Doses for excess cancer risks of approximately 5×10^{-6} or lower would be protective of neurodevelopmental effects since the RfD established on the basis of these effects is 7 µg/kg-day (see section 5.1.3). As explained above, there is some uncertainty in this slope factor because some of the neoplastic nodules might have been nonneoplastic hyperplasia rather than preneoplastic foci of cellular alteration or hepatic adenomas. The combination of the hyperplastic nodules and carcinomas for the dose-response analysis leads to a conservative but protective slope factor.

5.3.5. Previous Cancer Assessment

The carcinogenicity of decaBDE was evaluated in IRIS (U.S. EPA, 1989). DecaBDE was classified in Group C, "possible human carcinogen," according to EPA cancer guidelines (U.S. EPA, 1986b). The basis of this classification was lack of human carcinogenicity data and limited evidence of carcinogenicity in animals, namely, significantly increased incidences of neoplastic liver nodules in male and female rats and increased incidences of hepatocellular adenomas or carcinomas (combined) in male mice (NTP, 1986). A quantitative estimate of carcinogenic risk from oral exposure was not derived in the IRIS assessment because the final NTP (1986) report was not available at the time.

On the basis of the carcinogenicity studies in F344/N rats and B6C3F1 mice, NTP (1986) concluded that there was "some evidence of carcinogenicity" for male and female rats as shown by increased incidences of neoplastic nodules of the liver in low-dose males and high-dose groups of both males and females. There was "equivocal evidence of carcinogenicity" for male mice as shown by increased incidences of hepatocellular adenomas or carcinomas (combined) in the low-dose group and of thyroid gland follicular cell adenomas or carcinomas (combined) in both dosed groups. There was "no evidence of carcinogenicity" for female mice receiving low or high dose of decaBDE in the diet. Several nonneoplastic lesions were observed at increased incidences, the most notable being thyroid gland follicular cell hyperplasia in male mice.

The potential carcinogenicity of decaBDE was evaluated by NAS (2000) on the basis of the NTP (1986) study. Based on lack of human data and limited evidence of carcinogenicity in animals (i.e., significant increased incidences of neoplastic liver nodules in male and female rats and increased incidences of hepatocellular adenomas or carcinomas in male mice), NAS (2000) concluded that decaBDE is a possible carcinogen in rats but has not concluded that it is a carcinogen in humans. Based on the incidence of hepatic neoplastic nodules in male rats (NTP, 1986), a cancer slope factor of 9×10^{-4} per mg/kg-day was derived, applying the multistage model to censored data to adjust for differential mortality among treated rats.

6. MAJOR CONCLUSIONS IN THE CHARACTERIZATION OF HAZARD AND DOSE RESPONSE

6.1. HUMAN HAZARD POTENTIAL

Studies of toxicokinetics of decaBDE reveal that the chemical can be absorbed by the oral route to a limited extent, does not accumulate in tissues, and undergoes clearance, largely as a result of metabolism in the liver and excretion in the bile.

Short-term and subchronic studies demonstrated low toxicity from oral exposure to decaBDE with NOAELs of 3,000 mg/kg-day or higher. NTP (1986) conducted a chronic toxicity and carcinogenicity dietary study in F344 rats. DecaBDE caused an increase in the incidence of thrombosis in the liver in high-dose male rats (2,240 mg/kg-day). A dose-dependent, but insignificant, increase in the incidence of degeneration of the liver was also observed in treated male rats. In the spleen, a dose-dependent increase (statistically significant in the high-dose group) in the incidence of fibrosis was observed in males. In the mandibular lymph node, lymphoid hyperplasia increased in males in a dose-dependent manner, but the incidence reached statistical significance only at the high dose. Histopathology examination also revealed a dose-dependent increase in the incidence of neoplastic nodules in the liver in both male and female rats. Female rats appeared to be refractory to the systemic toxicity of decaBDE at the doses used in this study.

The observed toxicity of decaBDE in the 2-year study in rats is further supported by the 2-year mouse study conducted by NTP (1986). Significant increases in the incidence of centrilobular hypertrophy were observed in the liver of treated male mice. In the thyroid gland, a dose-dependent and statistically significant increase (at all dose levels) in the incidence of follicular cell hyperplasia was observed in male mice. In the females, the incidence increased in the low- and high-dose groups compared with the control group, but the increase was not statistically significant at any dose level. Female mice in the high-dose group exhibited a significant increase in the incidence of stomach ulcers. In addition, there were significant increases in the combined incidence of hepatocellular adenomas or carcinomas at both low and high doses in male mice. In the thyroid gland, follicular cell adenomas or carcinomas (combined) were slightly, but not significantly, increased in treated mice of both sexes. Similar to female rats, female mice appeared to be refractory to the systemic toxicity of decaBDE.

DecaBDE also has been shown to induce behavioral changes in several studies in mice and rats (Viberg et al., 2007, 2003a; Rice et al., 2007). In the principal study selected, Viberg et al. (2003a) investigated the neurotoxic effects of decaBDE on spontaneous motor behavior of adult NMRI male mice when these animals were exposed to a single oral dose as neonates on PND 3, 10, or 19 (i.e., at different stages of neonatal mouse brain development). Pair-wise testing between adult mice exposed on PND 3 and control groups indicated significant dose-related changes in all three spontaneous behavior variables at 2, 4, and 6 months of age. Adult mice exposed neonatally up to 20.1 mg on either PND 10 or 19 did not show any significant differences in any of the variables. These data suggested that there was a critical window for the induction of behavioral disturbances, and the neurotoxic effect of neonatal decaBDE exposure was persistent and also worsened with age in male mice.

The appropriate hazard descriptor for decaBDE is "suggestive evidence of carcinogenic potential" (U.S. EPA, 2005a, b). The weight-of-evidence of human carcinogenicity of decaBDE is based on (1) no studies of cancer in humans exposed to decaBDE; (2) a statistically significant increase in incidence of neoplastic nodules and a slight increase in incidence of carcinomas (not statistically significant) in the liver of low- and high-dose male rats and high-dose female rats; (3) a significantly increased incidence of hepatocellular adenoma or carcinoma (combined) in male mice at the low dose and marginally increased incidence at the high dose; (4) a nonsignificantly increased incidence of hepatocellular adenoma or carcinoma (combined) in female mice; (5) a slightly greater (but statistically not significant) incidence of thyroid gland adenomas or carcinomas (combined) in dosed male and female mice; (6) a significantly increased incidence in male mice, at both doses, of follicular cell hyperplasia, considered by many as a precursor to thyroid tumors; and (7) an apparent absence of genotoxic potential.

The weight of experimental evidence is on the strong end of the spectrum for the descriptor "suggestive evidence of carcinogenic potential," since there is suggestive evidence that decaBDE is carcinogenic for more than one species, sex, and site. Based on the weight of evidence, a dose-response assessment of the carcinogenicity of decaBDE is deemed appropriate.

6.2. DOSE RESPONSE

6.2.1. Noncancer/Oral

BMD modeling was conducted for all the potential critical effects observed in the rat and mouse chronic studies, including thrombosis in the liver, liver degeneration, fibrosis in the spleen, and lymphoid hyperplasia in male rats, as well as centrilobular hypertrophy in the livers and follicular cell hyperplasia in the thyroid of male mice. The data on neurobehavioral effects in the Viberg et al. (2003a) study could not be modeled because the data were presented graphically rather than numerically and thus were not amenable to BMD analysis. The lowest $BMDL_{10}$ in rodent chronic studies is 383 mg/kg-day for liver degeneration effect in male rats. This value is much higher than the NOAEL level of 2.22 mg/kg for the neurobehavioral changes observed in mice (Viberg et al., 2003a). Therefore, the NOAEL of 2.22 mg/kg is used as a point of departure for calculating the oral RfD. A composite UF of 300 was applied to this effect level to account for the interspecies uncertainty (10-fold), intraspecies variation (10-fold), and extrapolation of a single dose to a lifetime exposure (3-fold), yielding an RfD of 0.007 mg/kg-day or 7 μg/kg-day.

The available database included acute, short-term, subchronic, and chronic studies in two species. Also, there are developmental and reproductive studies (Tseng et al., 2006; Hardy et al., 2002) in addition to the critical neurobehavioral study. Confidence in the principal study (Viberg et al., 2003a) is low because the study used a single dose during a period of neurodevelopmental vulnerability. In addition, only limited tests on motor activity were conducted in only male mice in the critical study by Viberg et al. (2003a). This study is strengthened by the results of Rice et al. (2007), where behavioral effects were identified in neonatally exposed PND 70 mice following a repeated postnatal dose protocol, and also by the results of the Viberg et al. (2007) study in rats. The Viberg et al. (2003a) study provides information on the most sensitive endpoint; therefore, using the NOAEL from this study as a point of departure to calculate the RfD is expected to provide adequate protection for humans.

The overall confidence in the RfD assessment of BDE-209 is low.

6.2.2. Cancer/Oral

Although no human studies were available, two chronic rodent studies (NTP, 1986) provide suggestive evidence of decaBDE-induced carcinogenicity. The data from these studies are adequate to support a quantitative cancer dose-response assessment. There is very limited information exploring the mode of action for any of the tumors reported in the animal chronic studies. DecaBDE was not mutagenic or genotoxic in several in vitro studies, and there are no data to support a nongenotoxic mode-of-action hypothesis. In the absence of such data, extrapolation from the point of departure to lower doses is most appropriate using a linear approach.

Based on a comparison of estimated EDs for all the cancer endpoints observed in rat and mouse chronic studies (NTP, 1986), the neoplastic nodule or carcinoma (combined) in the treated rats is the most sensitive endpoint. Therefore, the LED_{12} of 178 mg/kg-day estimated for this endpoint is used as a point of departure for calculating the cancer slope factor. For neoplastic nodules or carcinomas (combined), the resulting oral cancer slope factor is 7×10^{-4} per mg/kg-day. This slope factor assumes that all neoplastic nodules were preneoplastic cellular changes with the potential to become malignant. Based on this slope factor, the doses associated with excess cancer risks of 10^{-4}, 10^{-5}, and 10^{-6} are approximately 100, 10, and 1 μg/kg-day, respectively. There is some uncertainty in this estimate, given the fact that the tissues identified as neoplastic nodules may have included some lesions now categorized as nonneoplastic hyperplasia (Maronpot et al., 1986).

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Viberg, H; Fredriksson, A; Eriksson, P. (2005) Deranged spontaneous behavior and decrease in cholinergic muscarinic receptors in hippocampus in the adult rat, after neonatal exposure to the brominated flame-retardant, 2,2',4,4',5-pentabromodiphenyl ether (PBDE 99). Environ Toxicol Pharmacol 20:283–288.

Viberg, H; Fredriksson, A; Eriksson, P. (2007) Changes in spontaneous behavior and altered response to nicotine in the adult rat, after neonatal exposure to the brominated flame retardant, decabrominated diphenyl ether (PBDE 209). Neurotoxicol 28:136–142.

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Wolf, DC; Mann, PC. (2005) Confounders in interpreting pathology for safety and risk assessment. Toxicol Appl Pharmacol 202:302–308.

Zhou, T; Ross, DG; DeVito, MJ; et al. (2001) Effects of short-term in vivo exposure to polybrominated diphenyl ethers on thyroid hormones and hepatic enzyme activities in weanling rats. Toxicol Sci 61:76–82.

APPENDIX A: SUMMARY OF EXTERNAL PEER REVIEW AND PUBLIC COMMENTS AND DISPOSITION

The "Toxicological Review" for BDE-209 has undergone a formal external peer review performed by scientists in accordance with EPA guidance on peer review (U.S. EPA, 2006a, 2000a). The external peer reviewers were tasked with providing written answers to general questions on the overall assessment and on chemical-specific questions in areas of scientific controversy or uncertainty. The external peer review for BDE-209 was conducted in concert with the external peer review of other PBDE congeners (i.e., BDE-47, BDE-99, and BDE-153), and some external peer review charge questions were specific to congeners other than BDE-209. External peer reviewer comments on all of the PBDEs and the Agency response are included below for completeness. A summary of significant comments made by the external reviewers and EPA's responses to these comments arranged by charge question follow. In many cases the comments of the individual reviewers have been synthesized and paraphrased in development of Appendix A. Synthesis of comments from individual peer reviewers resulted in summaries that combine similar statements from peer reviewers that were mentioned in conjunction with more than one charge question. In such cases, the comment and its response have been placed under the most relevant charge question. Some of the peer review comments were not directly related to charge questions. Those comments are categorized as miscellaneous and placed after those related to the charge questions. EPA also received scientific comments from the public. These comments and EPA's responses are included in a separate section of this appendix.

The peer review of the "Toxicological Review" for BDE-209 was coupled with the review of the documents for BDE- 47, -99, and -153. Accordingly, most of the charge questions address all four congeners. The responses to the charge questions in this appendix apply primarily to comments related to BDE-209. The charge to the external peer reviewers and final external peer review report (February 2007) pertaining to the toxicological reviews of the four polybrominated diphenyl ether congeners are available at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=161970. The public comments received can be found at http://www.regulations.gov/fdmspublic/component/main under the Docket EPA-HQ-ORD-2006-0838.

EXTERNAL PEER REVIEWER COMMENTS

The reviewers made several editorial suggestions to clarify specific portions of the text. These changes were incorporated in the document as appropriate and are not discussed further.

A. General Comments

Charge Question 1. *Are you aware of other published peer-reviewed toxicological studies not included in these toxicological reviews that could be of relevance to the health assessment of BDE-47, -99, -153, or -209?*

Comment 1: Three reviewers stated that they were unaware of any other relevant studies that would contribute to the BDE-209 IRIS assessment. One reviewer identified potentially relevant additional literature:

Jones-Ortazo, HA; et al. (2005) Environ. Sci. Technol. 39:5121-5130
Wilford, BH; et al. (2005) Environ. Sci. Technol. 39:7027-7035
Schecter, A; et al. (2005) J. Toxicol. Environ. Health Part A 68:501-513
Hites, RA; et al. (2004) Environ. Sci. Technol. 38:4945-4949
Schecter, A; et al. (2006) Environ. Health Perspect. 114:1515-1520
Fischer, D; et al. (2006) Environ. Health Perspect. 114:1581-1584
Bradman, A; et al. (2007) Environ. Health Perspect. 115:71-74
Kodavanti, PRS; Derr-Yellin, EC. (2002) Toxicol. Sci. 68:451-457
Kodavanti, PRS; et al. (2005) Toxicol. Sci. 88:181-192
Reistad, T; Mariussen, E. (2005) Toxicol. Sci. 87:57-65
Reistad, T; et al. (2006) Arch. Toxicol. 80:785-796

Response: The Agency reviewed and evaluated the studies recommended by the reviewer and has included the relevant studies for BDE-209. Fischer et al. (2006), Bradman et al. (2007), and Kodavanti et al. (2005) were found to be relevant and were added to the document. The remaining studies suggested by the reviewer fell outside the scope of the IRIS assessment (i.e., exposure data, commercial mixtures). Additionally, a new literature search was conducted to ensure that recently published relevant studies are included in the IRIS assessment. Four studies were added to the "Toxicological Review" for BDE-209 as the result of the literature search (Huwe and Smith, 2007; Pacyniak et al., 2007; Rice et al., 2007; Thuresson et al., 2006). A description of these studies can be found in sections 3 and 4.

B. Oral Reference Dose (RfD) Values

Charge Question 2. *Have the rationale and justification for deriving RfDs on the basis of the neurobehavioral toxicity studies been transparently and objectively described in the draft* *toxicological reviews of BDE-47, -99, -153, and -209? Are there additional studies that should be considered for deriving the RfDs for any of the four PBDE congeners?*

Comment 1: Three reviewers stated that the rationale for deriving the RfD based on the neurobehavioral toxicity studies was clearly and transparently described. Two reviewers stated that the neurobehavioral effects are the only toxic effects that have been observed consistently in PBDE rodent studies. One of these reviewers noted that, although the rat and mouse bioassays by NTP (1986) provide suitable data, the neurobehavioral studies appeared to provide the most appropriate dose-response data on which to base the health assessment. None of the reviewers suggested additional studies that should be considered for deriving the RfD.

Response: No response needed.

Charge Question 3. *Do you agree or disagree with EPA basing the health assessment of BDE-47, -99, -153, and -209 to a large extent on the Eriksson/Viberg neurobehavioral studies?*

Comment 1: One reviewer supported the use of the Eriksson/Viberg neurobehavioral study as the basis for the derivation of the RfD, given the limited body of toxicological information available. Two reviewers noted that the studies are limited by the fact that they originated from the same laboratory. One reviewer was concerned that the experimental design of the principal study selected more than one pup per litter, ignoring the "litter" effect. Treating littermates as independent experimental units could confuse dose effects with litter effects. Another reviewer was concerned with the specificity of the neurobehavioral data for developmental neurotoxicity and suggested that independent confirmation of the endpoints is essential. One peer reviewer identified the use of a single sex (male mice) as a limitation of the critical study that had not been identified in the "Toxicological Review" discussion of study limitations. One of these reviewers stated that these limitations do not hinder the derivation of the RfD for BDE-209 but make the confidence low. Another reviewer noted that the neurobehavioral findings of this laboratory have been corroborated in a study examining BDE-99 (Kuriyama et al., 2005). None of the reviewers stated that the studies could not be used as the basis for the derivation of the RfD.

Response: The "Toxicological Review" contains a detailed summary of the concerns with the study design and methods utilized in the principal study (see section 5.1.1). A discussion of the use of only male mice in the study by Viberg et al. (2003a) has been added to the discussion in section 5.1.1 of the "Toxicological Review." Additionally, the neurobehavioral effects reported in Viberg et al. (2003a) are supported by a study in male and female mice that was published by

Rice et al. (2007) after the peer review, which used an expanded array of neurodevelopmental endpoints and dosing for 14 days. The neurodevelopmental findings from Viberg et al. (2003a) are also supported by an expanding body of literature for the BDE-47, -99 and -153 congeners (Viberg et al., 2007, 2005, 2004a, b, 2003b, 2002; Kuriyama et al., 2005; Eriksson et al., 2002, 2001; Branchi et al., 2002) that details changes in motor and cognitive activity in rodents following administration of single or repeated perinatal doses of PBDEs. Some of the concerns associated with the methodology of the Eriksson/Viberg neurobehavioral studies are alleviated by other studies (Rice et al., 2007; Kuriyama et al., 2005; Branchi et al., 2002) using more traditional methodologies that have generated toxic effects similar to those reported by Viberg et al. (2003a). Results reported by Viberg et al. (2003a) for BDE-209 are similar to results reported by Eriksson et al. (2001) for BDE-47, Viberg et al. (2004b) and Kuriyama et al. (2005) for BDE-99, and Viberg et al. (2003b) for BDE-153. Altogether, these studies support the findings of Viberg et al. (2003a) that exposure to BDE-209 in early developmental stages can result in lasting changes in the neurobehavioral activity of mice.

Charge Question 4. *Are the Eriksson et al. (2001) (BDE-47), Viberg et al. (2004b) (BDE-99), Viberg et al. (2003b) (BDE-153), and Viberg et al. (2003a) (BDE-209) studies appropriate for determining the point of departure? Have the strengths and weaknesses of the Viberg and Eriksson studies been appropriately characterized and considered?*

Comment 1: All four reviewers believed that the Viberg et al. (2003a) BDE-209 study was appropriate for determining the point of departure. One reviewer felt that these data were appropriate as long as the document emphasizes that the neurochemical data also show alterations in normal developmental patterns. Another reviewer noted that both Viberg et al. (2003a) and NTP (1986) provided data appropriate for determining a point of departure, with Viberg et al. (2003a) providing the lowest point of departure. None of the reviewers suggested an alternative study for determining the point of departure. Two reviewers explicitly stated that the strengths and weaknesses were identified and clearly presented.

Response: No response needed.

Charge Question 5. *Have the most appropriate critical effect and point of departure been selected? And has the rationale for the point of departure been transparently and objectively described?*

Comment 1: All four reviewers agreed with the selection of the neurobehavioral effects as critical effects and that these effects were appropriate for identifying a point of departure. One of the reviewers felt that the neurochemical data also provided critical information and should be presented centrally rather than as supporting data. One reviewer stated that there was no correlation between PND of exposure and the concentration of the chemical in the brain. One reviewer added that decreased habituation might be as appropriate as or more appropriate than the habituation ratio as an indicator of toxicity, while another believed that the actual behavioral data, rather than the habituation ratio, should have been presented in the document. It was not clear for another reviewer why the actual data could not be recovered from the study authors to allow for dose-response modeling and BMD estimation, given that the studies were published fairly recently (2003). This reviewer recommended that the Agency attempt to recover the neurobehavioral toxicity data from the study authors.

Response: The evidence of neurochemical interactions and the potential relationship with the neurobehavioral effects are highlighted in the mode-of-action section of the document (section 4.5.3). The document presents the hypothesis proposed by the Eriksson/Viberg group in which the observed effects on locomotion and habituation are related to impaired development of the cholinergic system during the postnatal brain growth spurt; however, data are unavailable to determine the relevance of the neurochemical effects or to establish a mode of action. This conclusion has been added to section 4.5.3. In the case of BDE-209, the levels of radiolabel in the brain were higher following administration of equivalent doses on PND 3 or 10 compared to PND 19 (Viberg et al., 2003a). There are no measurements of levels of BDE-209 or the congeners in the brain or other tissues at the time of neurobehavioral testing at 2 or 4 months to show if any differences exist in the brain or other tissues at those time points.

The actual motor activity components (locomotion, rearing, and total activity) that gave rise to the habituation ratios were reported in graphical form only and could not be reasonably estimated as presented, and the Agency's attempts to obtain the raw data were unsuccessful. Thus, the habituation ratios, rather than the actual habituation data, served as the basis for determining the point of departure.

Comment 2: Two reviewers thought that the rationale for the point of departure had been transparently and objectively described. Another reviewer felt the document provided clear rationalization for the selection of the point of departure. None of the reviewers stated that the rationale for the point of departure was not appropriately described.

Response: No response needed.

Comment 3: One reviewer noted that a BMDL would be better than a NOAEL for deriving an RfD.

Response: The Agency recognizes that a NOAEL can be limiting since it is highly dependent on the doses selected and the sample size and does not account for the dose-response curve. Alternatively, a BMDL is more independent of study design, takes into account the dose-response curve, and, therefore, is preferable to a NOAEL as a point of departure. However, the data in the principal study for BDE-209 only allows for the identification of a NOAEL. The reporting is insufficient to provide the necessary information to perform BMD modeling and the Agency's attempts to obtain the raw data were unsuccessful.

Charge Question 6. *Have the rationale and justification for each UF selected in the draft toxicological reviews of BDE-47, -99, -153, and -209 been transparently described? If the selected UFs are not appropriate, what alternative UFs would you suggest and what are the scientific rationales for those suggested? Does the database support the determinations of the RfDs for BDE-47, -99, -153, and -209?*

Note: The peer reviewers provided fairly extensive comments about the individual components of the combined UF. For that reason the following reviewer comments and EPA responses have been grouped by the area of uncertainty to which they apply.

Comment 1: Two reviewers agreed that the document described the rationale and justification for each UF and another reviewer noted that the selection of the UFs was described in detail. The fourth reviewer felt that the document did not provide much explanation or justification for applying the default intraspecies UF_H for BDE-209.

Response: There is little information available on the effects of PBDEs in humans and in the absence of data there is no scientific rationale for moving away from the default value for the intraspecies UF_H. Additional explanation for the intraspecies UF_H was added to section 5.1.3.

Comment 2: One reviewer suggested decreasing the interspecies UF_A, considering the relatively specific and sensitive nature of the neurobehavioral and neurochemical measures compared with conventional endpoints. However, another reviewer felt that the 10-fold UF_A was justifiable based on the lack of data on the mode of action in animals and humans.

Response: The 10-fold UF_A for interspecies uncertainty is retained based on the lack of mode-of-action, pharmacokinetic, and human data that would sufficiently illustrate the similarities and differences for the effects of the PBDEs in animals and humans. Additional explanation for applying the default interspecies UF_A was added to section 5.1.3.

Comment 3: Two reviewers suggested lowering the intrahuman UF_H. One of these reviewers felt the relatively specific and sensitive nature of the neurobehavioral and neurochemical measures compared with conventional endpoints warranted a decrease in the UF_H. The other reviewer recommended decreasing the 10-fold UF_H to 3-fold based on the sensitivity of the test species population (neonates).

Response: The 10-fold UF_H for intraspecies uncertainty is retained based on the lack of information concerning the pharmacokinetics and mode of action of the BDE-209 in humans. In the absence of human data, the effects in potentially susceptible populations exposed to BDE-209 cannot be determined. Additional explanation for applying the default intraspecies UF_H was added to section 5.1.3.

Comment 4: One reviewer disagreed with the treatment of a single-dose experiment as equivalent to a subchronic exposure when applying a UF to account for differences in exposure duration. This reviewer stated that the principal study needs to be treated as a single-dose study and not a subchronic study. The reviewer also felt that the threefold UF_S was inappropriate and suggested raising the UF_S from 3 to 10 to consider the extent to which the mother's pre-pregnancy accumulated body burden would influence the developmental outcome, especially since these data are unavailable. One reviewer agreed with the application of a threefold UF_S, recognizing that for the observed neurobehavioral effects the timing of exposure is more critical than the duration of exposure. This reviewer regards the UF_S as accounting for uncertainty from lack of prenatal exposure rather than uncertainty regarding potential effects of chronic exposure. One reviewer suggested the threefold UF_S may not be necessary, considering that exposure during a window of susceptibility indicates that chronic exposure may not necessarily result in greater adverse effects.

Response: For BDE-209, the principal study identified endpoints that, for the most part, reflect specific aspects of developmental physiology. The hypothesized window of susceptibility, proposed by the study authors, is based on the observation that the developmental neurotoxic effects observed following exposure to BDE-209 on PND 3 will not occur once the toxicokinetics of intestinal uptake and excretion have matured and the animal brain is developmentally less active (outside the window of susceptibility). The Eriksson/Viberg group has suggested that the period of maximum vulnerability for the developing cholinergic system that coincides with the most pronounced neurodevelopmental effects from BDE-99 exposure is from PNDs 10–14. However, for BDE-209 the developmental neurotoxic effects were noted following exposure on PND 3 rather than on PNDs 10 or 19. It is likely that two factors contributed to this difference in peak vulnerability. First, absorption from the gastrointestinal tract decreases as the neonatal mice age during their first few weeks of life, thus less of the BDE-209 reaches the liver for distribution on PNDs 10 and 19 than on PND 3. Secondly, distribution to the brain is slow. The amount of radiolabel in the brain is 1.4- and 2.8-fold greater 7 days after dosing compared with 24 hours after dosing on PNDs 3 and 10, respectively. Even less reaches the brain when the BDE-209 is administered on day 19. The UF_S was viewed as a dosing duration adjustment rather than simply a comparison of the effects of a subchronic to a chronic exposure. A threefold UF_S was applied because the critical study dosed the animals only once within the hypothesized critical window, not because the chronic exposures would have exacerbated the impact on habituation.

In response to the comment about possible effects as the result of a maternal pre-pregnancy body burden, the Agency notes that, although the principal study did not include prenatal exposure, the maternal uptake and retention of BDE-209 during the prenatal period would be lower than that of the pups during the postnatal period of vulnerability because of the differences in toxicokinetics for mature versus neonatal animals. Support for the UF_S is provided by the Hardy et al. (2002) study, where BDE-209 treatment did not produce any evidence of maternal or developmental toxicity up to the highest dose tested (1,000 mg/kg-day) despite exposure from gestation days 0 through 19.

Comment 5: Two reviewers recommended raising the onefold database UF_D to threefold. One of these reviewers based this decision on the use of a NOAEL rather than a BMDL as the point of departure. This reviewer felt that the absence of definitive data for dose-response modeling for the neurobehavioral effects reflects an inadequacy in the database, although if the endpoints could be modeled then a onefold UF_D is acceptable. The other reviewer suggested raising the UF_D to account for the lack of other developmental neurotoxicity studies.

Response: EPA's practice is to apply a database UF_D, generally ranging from 1–10, in the health assessment to account for the potential for deriving an underprotective RfD as a result of an incomplete characterization of a chemical's toxicity because of missing studies. In deciding to apply this factor to account for deficiencies in the available data set and in identifying its magnitude, EPA considers both the data lacking and the data available for particular organ systems as well as life stages. The database for BDE-209 contains subchronic and chronic toxicity studies as well as a traditional developmental study. Although the database lacks a two-generation reproductive study, the absence of effects in the available longer-term and developmental studies indicates that at least some aspects of reproductive organ toxicity or function are not affected at doses much higher than those that resulted in the neurological effects observed in neonates in the principal study. Therefore, the Agency retains the onefold database

UF_D. Calculating a BMDL rather than using a NOAEL for the point of departure would not impact the use of a database UF.

Comment 6: Two reviewers believed the database supports the determination of the RfD but stated that the overall confidence in the RfD assessment is low. Another reviewer believed the database is very poor and suggested that the RfDs be acknowledged as temporary while waiting for additional studies that increase confidence.

Response: The statement that the overall confidence in the RfD is low is included in the "Toxicological Review" in section 6.2. The Agency does not develop temporary RfDs for IRIS assessments. However, the availability of new information is one of the factors considered in selecting a chemical for reassessment.

C. Body Burden Approach

Charge Question 7. *Are there adequate data for considering body burden as an alternative dose metric to administered doses in any of the RfD derivations?*

Comment 1: All four reviewers agreed that the data were inadequate to consider body burden as an alternative dose metric for the derivation of the RfD. Two of the reviewers stated that body burden is a possible alternative but the data are too limited.

Response: EPA examined the data on BDE-209 to determine if a body burden approach could be used for this congener during the development of the "Toxicological Review." It was determined that existing half-life, exposure, metabolite and mode-of-action data could not support a body burden calculation for this congener.

Charge Question 8. *Do you agree with the rationale described in the "Toxicological Review" of BDE-209 that the data on the window of susceptibility of the cholinergic receptors to BDE-209 tend to minimize body burden concerns?*

Comment 1: Three reviewers stated that the question was unclear. One reviewer accepted the concept as a basis for the experimental design, given the available information. A second reviewer stated that there was no direct evidence that BDE-209 directly affects cholinergic receptors and suggested that the mechanism of the interaction must be complex and indirect. A third reviewer stated that although there are no definitive data on mode of action, this hypothesis is plausible. This reviewer acknowledges that the data on the window of susceptibility of the cholinergic receptors to BDE-209 are suggestive but believes there are too many other possibilities for mode of action for this rationale to minimize body burden concerns.

Response: Available mode-of-action data that describe the developmental neurotoxicity of BDE-209 are limited. The Eriksson/Viberg group, the principal study authors, have hypothesized that the observed effects on locomotion and habituation are related to impaired development of the cholinergic system during the postnatal brain growth spurt period based on studies of BDE-99 (Viberg et al., 2005, 2004a) and supported by studies with BDE-153 (Viberg et al., 2003b) and BDE-209 (Viberg et al, 2007, 2003a). They have further hypothesized that the sensitivity of the cholinergic system occurs in the vicinity of PND 10 and have tested this hypothesis by varying the time of dosing and observing differences in the habituation effect for BDE-99 and BDE-209 (Viberg et al., 2007; Eriksson et al., 2002). A difference in the impact of the time of dosing was observed between BDE-99 and BDE 209 and can be explained based on toxicokinetic factors (see section 4.5.3). The resulting deficit in cholinergic receptors persisted across the duration of testing and could cause an abnormal response to exposure to cholinergic stimulants in adulthood. The following statement has been added to the mode-of-action summary (section 4.5.3): "While evidence exists that demonstrates BDE-209, as well as other PBDEs, interacts at the neurological level, data are inadequate to determine the mode of action for BDE-209."

D. Carcinogenicity Assessment

Charge Question 9. *Is the weight of evidence for the carcinogenicity of BDE-209 in the draft "Toxicological Review" appropriately described? Are there additional studies that should be included?*

Comment 1: Three reviewers commented that the weight of evidence for carcinogenicity of BDE-209 was appropriately described in the "Toxicological Review." One reviewer stated that the carcinogenicity study was completely and methodically described. This reviewer noted that the carcinogenicity study is over 25 years old and utilized very high doses that led to some toxic effects and animal deaths. None of the reviewers were aware of additional studies that should be included in the cancer assessment for BDE-209.

Response: No response needed.

Charge Question 10. *Do the data support estimation of a cancer slope factor for BDE-209? If yes, is the rationale for the quantitative analysis objectively and transparently described,* *considering the uncertainty in the data and the suggestive nature of the weight of evidence? Have the rationale and justification for the use of the linear low-dose extrapolation been objectively and transparently presented?*

Comment 1: One reviewer stated that the data appear to support estimation of a cancer slope factor, one reviewer stated that the data supports estimation, one reviewer did not specifically answer this question but, as mentioned below, did question the appropriateness of the study EPA used, and the fourth reviewer did not answer the question about the support for estimation of a cancer slope factor. One reviewer felt that the data supported the weight-of-evidence classification as "suggestive of the carcinogenic potential." One reviewer questioned the appropriateness of the NTP (1986) study for developing the cancer slope factor based on the utilization of very high doses and potentially limited absorption of BDE-209 and suggested that a new bioassay be conducted. This reviewer recognized the public comments on the carcinogenesis data, particularly the statements regarding the modest dose-response and the change, since the completion of the study, in criteria for classifying liver lesions in rats. This reviewer was less concerned with the scoring of neoplastic nodules as tumors because the nodules identified in chronic studies with exposure to a single compound are less likely to regress as compared with an initiation/promotion study. Regarding the change in classification criteria, another reviewer noted that the data supported the estimation of a cancer slope factor for BDE-209, with the assumption that the change in classification of the neoplastic nodules would not appreciably change the dose response. Two reviewers explicitly stated that the rationale for the quantitative analysis is transparently described. Two reviewers stated that the justification for the use of the linear low-dose extrapolation is objectively presented in the BDE-209 assessment. One reviewer noted that the document did not include a rationale or justification, other than a reference to EPA guideline documents (U.S. EPA, 2005a, b), for the use of linear low-dose extrapolation. None of the reviewers disagreed with the estimation of the cancer slope factor or the use of linear low-dose extrapolation.

Response: The Agency is aware of the deliberations concerning the significance of neoplastic nodules in interpreting cancer risk. In 1986, a significant change was made regarding the NTP nomenclature for hepatoproliferative lesions of rats: lesions previously combined under the diagnosis of "neoplastic nodules" were replaced with three terms: "hepatocellular hyperplasia," "foci of cellular alteration," and "hepatocellular adenoma." The term "hyperplasia" was reserved for proliferative lesions that were perceived to be secondary, nonneoplastic responses to degenerative changes in the liver. Foci of cellular alteration, hepatocellular adenoma, and hepatocellular carcinoma were considered to represent a spectrum of changes that are part of the carcinogenic process (Maronpot et al., 1986). It is recognized that not all neoplastic nodules have the potential to progress to malignancy: some neoplastic nodules may regress following removal of a chemical stimulus, others may only be hyperplastic lesions, and still others may progress to hepatocellular carcinoma. Therefore, the exact contribution of neoplastic nodules to the overall incidence of carcinoma in the rat liver is not known with any certainty. However, an increase in neoplastic nodules in treated rats provides some indication that the liver may be at increased risk of cancer formation, and inclusion of the incidence of neoplastic nodules in the assessment of cancer risk is considered to be a conservative approach (U.S. EPA, 1986c). This change in nomenclature has been noted in the "Toxicological Review" in sections 4.2, 4.6.2, and 5.3.3 and in Table 4-2.

EPA acknowledges that toxicokinetic limitations on solubility and absorption may make external dose a poor indicator of systemic dose. However, there are no PBPK models for BDE-209 that might be used to estimate internal dose. Thus, the only parameter available for modeling dose-response is the external dose.

The justification for using the linear low-dose extrapolation for deriving a cancer slope factor for BDE-209 is based on the absence of data available to determine the mode of action for BDE-209. This rationale is provided in section 5.3.4.

Charge Question 11. *Are there alternative modeling approaches that should have been considered instead of or in addition to the linear low-dose extrapolation approach?*

Comment 1: None of the reviewers suggested that an alternative modeling approach should have been considered. One reviewer stated that all possible modeling approaches were explained and the model that best fit the experimental data was selected. Another reviewer noted that consideration of other modeling approaches is not necessary, considering the dose-response data are linear, the linear model adequately fits the data, and the data are inadequate to justify an alternative approach.

Response: No response needed.

Miscellaneous Comments

Comment 1: Three reviewers felt that the assessment would benefit from the combination of the individual documents for the four congeners into one comprehensive document to compare and cohesively present the similarities and differences among the congeners.

Response: The Agency has recently completed IRIS assessments for four individual PBDE congeners: BDE-47, -99, -153, and -209 (see Foreword). These congeners were selected based on frequent detection in human tissues and the environment, availability of animal toxicological studies suitable for human health assessment, and their common occurrence in commercial PBDE mixtures. Although there is some repetition in the four documents, the available database is sufficiently different from one congener to another to support the separation of the four IRIS assessments. However, in response to the comments from the peer reviewers, the Agency has increased the text that compares the data on BDE-209 to those of the other congeners evaluated using comparable methodological approaches.

Comment 2: One reviewer noted that the document failed to cite the purities of the radioactive chemicals in most of the studies, the position of the label, location of radioactivity in the brain, and the specific activities of the ^{14}C compounds. Another reviewer questioned the reliance upon the ^{14}C data and the intermixing with direct chemical measures. The reviewer felt that the conclusions drawn were challenging.

Response: The requested data were added to the descriptions of the pertinent studies (in section 3) when they were provided by the authors of the paper. Frequently, the position of the radiolabel was not specified. In a few cases the radiolabel was described as "uniform," suggesting that all carbons carried the radiolabel. If the authors of the paper used the term "uniform," it has been added to the discussion of the study. No change was made if the authors of the paper did not comment on the position of the radiolabel.

Comment 3: One reviewer was concerned that the doses and concentrations of the compound and the metabolites in biological tissues were presented in differing units (i.e., μmol, μg, percent of dose).

Response: Doses and concentrations are reported as given by the authors. If a dose was given in molar or mole units per unit body weight, the doses have been provided parenthetically as mg/kg body weight values. Otherwise the units are those provided in the published papers.

Comment 4: One reviewer suggested including proposed metabolic pathways to strengthen the fact that the lower brominated congeners could be obtained from the higher brominated ones.

Response: A diagram of a proposed metabolic pathway has been included as Figure 3-1 in section 3.3. The diagram is based on the metabolites that have been identified in several studies. The metabolic pathway is described as "proposed" and uncertainties are indicated. The individual publications that provided data on metabolites are cited in the Figure 3-1. In cases where the data from one study are discussed in more than one section of the "Toxicological Review," a reference to the location of prior mention of the study is provided.

Comment 5: One reviewer acknowledged that developmental neurotoxicity is consistently observed following exposure to the PBDEs despite very different patterns of metabolism, distribution, and persistence within the body. This reviewer recommended rationalizing the relative potency of the PBDEs, considering the differences in the extent of metabolism.

Response: Information is currently insufficient to identify the relative potency of the four congeners.

Comment 6: One reviewer suggested that the Agency provide conclusions on the extent of metabolism and the presence of metabolites in excreta for the PBDEs or provide a statement if conclusions cannot be drawn. One reviewer suggested the addition of a summary at the beginning of the toxicokinetics section to reduce potential confusion.

Response: An overview to the toxicokinetics section and summary paragraphs have been added to section 3.

Comment 7: One reviewer recommended improving the discussion of the possible debromination of BDE-209 to lower brominated congeners and questioned if environmental debromination should be mentioned.

Response: Discussion of the potential debromination of BDE-209 to lower-brominated congeners can be found in sections 3.2.2 and 3.3, based on evidence observed in several studies (Huwe and Smith, 2007; Morck et al., 2003; Sandholm et al., 2003; Zhou et al., 2001). Data for environmental debromination falls outside the scope of the IRIS health assessment.

Comment 8: One reviewer recommended presenting the receptor site interaction information in a summary table.
Response: Tables were added to the toxicological reviews for BDE-47, -99, and -153 because there were data for multiple congeners for the tetra, penta, and hexa congeners. In the case of BDE-209, there is only one PBDE congener and there was no need to have a table to summarize the data.

Comment 9: One reviewer felt that the evolution of exposures that are different in the U.S. compared with other countries and the pattern of exposures are important issues and the studies need to be presented to support or refute these observations.

Response: The Agency has provided information on exposure in the U.S. and other countries for comparison purposes. While the Agency agrees that exposure analysis is a critical component of risk assessment, a comprehensive presentation and analysis of exposure data are outside the scope of the IRIS health assessment.

Comment 10: One reviewer stated that the large number of bromine atoms of the PBDEs can impart electrophilic and lipophilic properties to the aromatic ring of the chemical and also noted that oily vehicles (e.g., corn oil) were used in most of the in vitro and in vivo animal studies. This reviewer was concerned the vehicle could significantly alter the distribution and tissue uptake of the PBDEs between the oily vehicle and the biological system. These conditions could lead to decreased absorption and distribution with subsequent alteration in metabolism and excretion.

Response: The lipohilicity of the BDE-209 is acknowledged in the "Toxicological Review" as part of section 3 on toxicokinetics. It will be necessary to determine if absorption occurs via the chylomicrons along with the body lipids or via direct membrane transport before the full impact of the vehicle on absorption, distribution, metabolism, and elimination can be determined. The data are currently inadequate to determine the impact of the oily vehicle on the distribution and uptake of BDE-209.

PUBLIC COMMENTS

The public commenters made several editorial suggestions to clarify specific portions of the text. These changes were incorporated in the document as appropriate and are not discussed further.

Comment 1: One public commenter suggested that the Agency consider a body burden approach.

Response: The Agency presented this issue to the peer reviewers in the form of a charge question. In response to the charge question about use of a body burden approach for dose evaluation, the peer reviewers agreed that, whereas the body burden approach might be appropriate for some of the congeners given their lipophilicity and distribution to adipose tissue, data to support such an approach are not presently available.

Comment 2: Three public commenters from one group questioned the selection of Viberg et al. (2003a) as the principal study for the derivation of the RfD, and another public commenter disagreed with the selection of Viberg et al. (2003a). Critiques of the study were submitted by the three public commenters questioning the methods utilized by the principal study authors. These public commenters were concerned that the purity of the radiolabeled BDE-209 in Viberg et al. (2003a) was not reported and suggested that observed effects may have been induced by impurities rather than the parent compound. Two of these public commenters felt that applying the intraspecies UF_H to account for sensitive populations when evidence for a sensitive subpopulation does not exist is overly conservative. One of the public commenters noted the use of inconsistent units of concentration within the document.

Response: The Agency has included a detailed summary of the concerns with the experimental design and methods utilized in the principal study (see section 5.1.1). These issues were raised during the external peer review of the BDE-209 IRIS assessment. The peer reviewers acknowledged the limitations and concerns with the study; however, all of the peer reviewers agreed that this study was appropriate for derivation of the RfD for BDE-209 and that its limitations were transparently discussed in the "Toxicological Review." Additionally, the neurobehavioral effects reported in Viberg et al. (2003a) are supported by other data for BDE-209 (Rice et al., 2007) and by an expanding body of literature for the PBDEs (Viberg et al., 2007, 2005, 2004a, b, 2003b, 2002; Kuriyama et al., 2005; Eriksson et al., 2002, 2001; Branchi et al., 2002) that details changes in motor and cognitive activity in rodents following administration of single or repeated perinatal doses of PBDEs. A summary of Rice et al. (2007) has been added to the BDE-209 "Toxicological Review" in section 4.3.2.

In response to the radiolabel concerns, the purities and positions of the radiolabels, the specific activities of the ^{14}C compounds, and the locations of radioactivity in the brain were added to the descriptions of the relevant studies (in section 3) when they were provided by the authors of the paper. Frequently, the position of the radiolabel was not specified and/or the radiolabel was inadequately described to allow for the detailed reporting. These data have been added to the document where available.

The 10-fold UF_H for intraspecies uncertainty is retained based on the lack of information concerning the pharmacokinetics and mode of action of the PBDEs in humans. In the absence of human data, the effects in potentially susceptible populations exposed to PBDEs cannot be determined. Additional explanation for applying the default intraspecies UF_H was added to section 5.1.3.

In response to the statement regarding the inconsistent reporting of units of concentration, the Agency notes that the doses and concentrations that are in the "Toxicological

Review" are reported as given by the authors. If a dose was given in molar or mole units per unit body weight, the doses have been provided parenthetically as mg/kg body weight values. Otherwise the units are those provided in the published papers.

Comment 3: One public commenter suggested a revision of the absorption, distribution, metabolism, and elimination sections (section 3) of the IRIS assessment for BDE-209. Additionally, another public group identified weaknesses in several studies within section 3.

Response: The toxicokinetics section (section 3) has been revised and updated to reflect recently published literature (Huwe and Smith et al., 2007; Pacyniak et al., 2007; Thuresson et al., 2006). An introduction to the toxicokinetics information has been added to section 3. The studies within this section have been reorganized to separate animal and human data in section 3.1.

Comment 4: One public commenter disagreed with the conclusion that the database for BDE-209 provides "suggestive evidence of carcinogenic potential." This commenter recommended adding a chronic study in rats administered BDE-209 (Kociba et al., 1975). Additionally, the public commenter noted the change in nomenclature for hepatoproliferative liver lesions in rats and the appropriateness of using the incidence of "neoplastic nodules" for quantitative cancer risk assessment.

Response: The external peer reviewers were asked to evaluate the weight of evidence for carcinogenic potential for BDE-209 and to determine if the database supported the estimation of a cancer slope factor. Three of the peer reviewers explicitly stated that the database was sufficient, and none of the reviewers disagreed with either the classification of "suggestive evidence of carcinogenic potential" or the quantitative cancer assessment for BDE-209. Kociba et al. (1975) administered a commercial grade BDE-209 that possesses a lower purity than the analytical grade utilized in the majority of the studies described in the IRIS health assessment. This study was not included for comparison since it falls outside the scope of the IRIS health assessment for the pure BDE-209 congener. Please see the response to the external peer review Comment 1, under Charge Question 10, regarding the change in criteria for the classification of hepatoproliferative liver lesions.

APPENDIX B: BENCHMARK DOSE ANALYSIS OF NONCANCER ENDPOINTS

The following data sets from the NTP (1986) 2-year rat and mouse studies were selected for BMD modeling: thrombosis in the liver, liver degeneration, fibrosis in the spleen, and lymphoid hyperplasia in male rats, as well as centrilobular hypertrophy in the liver and follicular cell hyperplasia in the thyroid of male mice.

BMD modeling was conducted by using EPA's BMDS, version 1.3.2. All the BMD analyses were conducted with the BMR set to a 10% response (U.S. EPA, 2000b). For each data set, all the available dichotomous models, including gamma, logistic, log-logistic, multistage, probit, log-probit, quantal-linear, quantal-quadratic, and Weibull, available in the BMDS were used. BMD model fit was evaluated based on the goodness-of-fit *p* value (indicating global model fit), local chi-square residual (indicating the model fit at the data point close to the preset BMR), as well as AIC (indicating model fit when controlling for number of model parameters). Based on the model output, the model(s) providing best model fit to the data were selected to estimate BMD_{10} and $BMDL_{10}$. In some cases, the BMDS gives exactly the same results for several different models. This occurs when model parameters are fixed at a boundary, yielding reduced models that are identical expressions for the probability of response. For example, when the power parameter in the Weibull or gamma model is fixed at 1 by BMDS or when the degree of the multistage model is set to 1 by the user, these models reduce to the quantal linear model. When this occurred, all the reduced models providing the same BMD results were considered as one model.

Liver Thrombosis in Male Rats

The data (1/50, 0/50, and 9/49 for control, low dose, and high dose, respectively) on thrombosis in the liver of male rats treated with decaBDE (NTP, 1986) were modeled with EPA BMDS. The reported oral doses were 0, 1,120, and 2,240 mg/kg-day, respectively. The data were modeled with all the dichotomous models available in the BMDS, and modeling results are summarized in Table B-1.

Based on these results, the models that did not demonstrate significant lack of fit for the data were obtained from three models (shown in bold in the table): gamma, log-logistic, and Weibull. These models provided relatively high goodness-of-fit *p* values and low AIC values. Based on these considerations, an average value of the BMDs estimated from these three models is used. For thrombosis in the livers of male rats, the average BMD_{10} is 2,125 mg/kg-day and the average $BMDL_{10}$ is 1,738 mg/kg-day.

Table B-1. Summary of BMD modeling results for thrombosis in the liver of male rats

Model	Goodness-of-fit p value	AIC	BMD$_{10}$	BMDL$_{10}$
Gamma	0.31	61.9754	**2,047**	**1,717**
Log-logistic	0.32	61.9384	**2,161**	**1,741**
Logistic	0.04	65.0449	1,909	1,597
Multistage	0.07	66.1380	1,898	1,449.97
Log-probit	N/A[a]	63.9383	2,130	1,691.4
Probit	0.04	65.8039	1,869	1,513.96
Quantal-linear	0.02	69.4028	2,030	1,162.71
Quantal-quadratic	0.07	66.1380	1,898	1,449.97
Weibull	0.31	61.9384	**2,166**	**1,757**

[a] N/A = not applicable.

Source: NTP (1986).

Liver Degeneration in Male Rats

The data (13/50, 19/50, and 22/49 for control, low dose, and high dose, respectively) on degeneration in the liver of male rats treated with decaBDE (NTP, 1986) were modeled with EPA BMDS. The reported oral doses were 0, 1,120, and 2,240 mg/kg-day, respectively. The data were modeled with all the dichotomous models available in the BMDS, and modeling results are summarized in Table B-2.

Table B-2. Summary of BMD modeling results for degeneration in the liver of male rats

Model	Goodness-of-fit p value	AIC	BMD$_{10}$	BMDL$_{10}$
Gamma	0.83	195.178	**779**	**422**
Log-logistic	0.89	195.148	**707**	**344**
Logistic	0.71	195.269	929	600
Multistage	0.83	195.178	**779**	**422**
Log-probit	0.51	195.555	1,161	718
Probit	0.72	195.259	914	584
Quantal-linear	0.83	195.178	**779**	**422**
Quantal-quadratic	0.42	195.779	1,363	962
Weibull	0.83	195.178	**779**	**422**

Source: NTP (1986).

Based on the goodness-of-fit p value, none of the models demonstrated lack of fit. The best model fit for the data was obtained from five models (shown in bold in the table): gamma, log-logistic, multistage, quantal-linear, and Weibull. These models provided high goodness-of-fit *p* values and low AIC values. However, among the five models, gamma, multistage, quantal-linear, and Weibull were reduced to a single identical model. Based on these considerations, an average value of the BMDs estimated from the log-logistic model and the common reduced model are used. For degeneration in the livers of male rats, the average BMD_{10} is 765 mg/kg-day and the average $BMDL_{10}$ is 406 mg/kg-day.

Liver Degeneration in Male Rats (NTP, 1986)
10% BMR

```
 ====================================================================
              Log-Logistic Model $Revision: 2.1 $ $Date: 2000/02/26 03:38:20
$
              Input Data File: C:\BMDS\DATA\RATS.(d)
              Gnuplot Plotting File:  C:\BMDS\DATA\RATS.plt
                                                  Thu Nov 25 12:11:49 2004
 ====================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:

P[response] = background+(1-background)/[1+EXP(-intercept-slope*Log(dose)]

Dependent variable = resp1
Independent variable = Dose
Slope parameter is restricted as slope >= 1

Total number of observations = 3
Total number of records with missing values = 0
Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

User has chosen the log transformed model

Default Initial Parameter Values
background   =    0.26
intercept    =    -8.66331
slope        =    1

Asymptotic Correlation Matrix of Parameter Estimates

( ~~*** The model parameter(s)  -slope have been estimated at a boundary point,~~
or have been specified by the user, and do not appear in the correlation
matrix )

background  intercept

background       1     -0.69

intercept        -0.69 1
```

```
Parameter Estimates
 Variable                  Estimate                  Std. Err.
 background                0.262212                  0.0603288
 intercept                 -8.75859                  0.569357
 slope                     1                         NA

NA - Indicates that this parameter has hit a bound implied by some inequality
constraint and thus has no standard error.

Analysis of Deviance Table
 Model            Log(likelihoo   Deviance        Test DF         P-value
                  d)
 Full model       -95.5647
 Fitted model     -95.5739          0.0184518     1               0.8919
 Reduced model    -97.5646         3.99968        2               0.1354

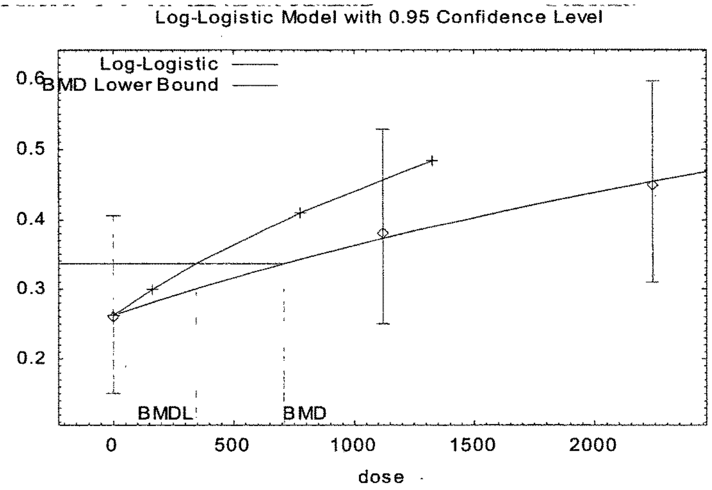
          AIC:          195.148

Goodness of Fit                                         Scaled
 Dose          Est._Prob     Expected      Observed     Size          Residual
 0.0000        0.2622        13.111        13           50            -0.03556
 1120.0000     0.3726        18.630        19           50            0.1081
 2240.0000     0.4543        22.259        22             49          -0.07432

Chi-square =        0.02     DF = 1        P-value = 0.8919

Benchmark Dose Computation
Specified effect        =     0.1
Risk Type         =     Extra risk
Confidence level  =     0.95

BMD         =     707.234
BMDL        =     344.083
```



12:11 11/25 2004

Splenic Fibrosis in Male Rats

The data (5/49, 8/50, and 13/49 for control, low dose, and high dose, respectively) on fibrosis in the spleen of male rats treated with decaBDE (NTP, 1986) were modeled with EPA BMDS. The reported oral doses were 0, 1,120, and 2,240 mg/kg-day, respectively. The data were modeled with all the dichotomous models available in the BMDS, and modeling results are summarized in Table B-3.

Table B-3. Summary of BMD modeling results for fibrosis in the spleen of male rats

Model	Goodness-of-fit *p* value	AIC	BMD_{10}	$BMDL_{10}$
Gamma	N/A[a]	139.172	1,464	700
Log-logistic	N/A	139.172	1,463	644
Logistic	0.92	137.183	**1,427**	**1,018**
Multistage	0.69	137.336	1,236	690
Log-probit	0.87	137.197	**1,519**	**1,017**
Probit	0.88	137.195	**1,393**	**968**
Quantal-linear	0.69	137.336	1,236	690
Quantal-quadratic	0.80	137.233	1,612	1,176
Weibull	N/A	139.172	1,470	700

[a]N/A = not applicable.

Source: NTP (1986).

Based on these results, the logistic, multistage, log-probit, probit, quantal-linear, and quantal-quadratic models did not show significant lack of fit for the data. The lowest AIC values were obtained with three models: logistic, log-probit, and probit (shown in bold in the table). Based on these considerations, an average value of the BMDs estimated from these three models is used. For fibrosis in the spleen of male rats, the average BMD_{10} is 1,446 mg/kg-day and the average $BMDL_{10}$ is 1,001 mg/kg-day.

Lymphoid Hyperplasia in Male Rats

The data (4/50, 6/50, and 13/49 for control, low dose, and high dose, respectively) on lymphoid hyperplasia in male rats treated with decaBDE (NTP, 1986) were modeled with EPA BMDS. The reported oral doses were 0, 1,120, and 2,240 mg/kg-day, respectively. The data were modeled with all the dichotomous models available in the BMDS, and modeling results are summarized in Table B-4.

Based on these results, the models that adequately fit the data were the logistic, multistage, probit, quantal-linear, and quantal-quadratic. The quantal-quadratic model (shown in bold in the table) provided a relatively high goodness-of-fit *p* value and the lowest AIC value.

Based on these considerations, the BMD and BMDL estimates from this model are selected. For lymphoid hyperplasia of male rats, the BMD_{10} is 1,538 mg/kg-day and the $BMDL_{10}$ is 1,165 mg/kg-day.

Table B-4. Summary of BMD modeling results for lymphoid hyperplasia in male rats

Model	Goodness-of-fit *p* value	AIC	BMD_{10}	$BMDL_{10}$
Gamma	N/A[a]	127.266	1,601	765
Log-logistic	N/A	127.266	1,608	725
Logistic	0.62	125.512	1,404	1,063
Multistage	0.36	126.122	1,207	707
Log-probit	N/A	127.266	1,575	1,032
Probit	0.57	125.59	1,364	1,007
Quantal-linear	0.36	126.122	1,207	707
Quantal-quadratic	0.86	125.298	**1,538**	**1,165**
Weibull	N/A	127.266	1,620	765

[a] N/A = not applicable.

Source: NTP (1986).

Centrilobular Hypertrophy in the Livers of Male Mice

~~The data (0/50, 34/50, and 32/50 for control, low dose, and high dose, respectively) on~~ centrilobular hypertrophy in the liver of male mice treated with decaBDE (NTP, 1986) were modeled with EPA BMDS. The reported oral doses were 0, 3,200, and 6,650 mg/kg-day, respectively. The data were modeled with all the dichotomous models available in the BMDS, and modeling results are summarized in Table B-5.

Table B-5. Summary of BMD modeling results for centrilobular hypertrophy in the liver of male mice

Model	Goodness-of-fit *p* value	AIC	Local chi-square residual	BMD_{10}	$BMDL_{10}$
Gamma	0.005	140.455	2.48	479	389
Log-logistic	0.094	134.65	1.44	258	180
Logistic	0	166.133	3.87	1,286	1,046
Multistage	0.005	140.455	0.7	479	389
Log-probit	0.004	140.591	2.22	839	676
Probit	0	165.095	4.03	1,253	1,036
Quantal-linear	0.005	140.455	2.48	479	389
Quantal-quadratic	0	164.89	5.08	1,612	1,451
Weibull	0.005	140.455	2.48	479	389

Source: NTP (1986).

Based on the BMD modeling results from all the models used, none of the available dichotomous models in the BMDS provided satisfactory data fit because all the goodness-of-fit *p* values are less than 0.1. This unsatisfactory model fit is due to the nonmonotonic dose response for this particular endpoint. Therefore, BMD and BMDL estimated from these model fits cannot be used.

Follicular Cell Hyperplasia in the Thyroid of Male Mice

The data (2/50, 10/50, and 19/50 for control, low dose, and high dose, respectively) on follicular cell hyperplasia in the thyroid of male mice treated with decaBDE (NTP, 1986) were modeled with EPA BMDS. The reported oral doses were 0, 3,200, and 6,650 mg/kg-day, respectively. The data were modeled with all the dichotomous models available in the BMDS, and modeling results are summarized in Table B-6.

Table B-6. Summary of BMD modeling results for follicular cell hyperplasia in the thyroid of male mice

Model	Goodness-of-fit *p* value	AIC	Local chi-square residual	BMD$_{10}$	BMDL$_{10}$
Gamma	N/A[a]	139.241	0	2,040	1,196
Log-logistic	N/A	139.241	<0.01	2,089	1,008
Logistic	0.34	138.147	0.70	2,989	2,430
Multistage	0.76	137.337	–0.09	**1,670**	**1,190**
Log-probit	0.66	137.436	0.34	2,561	1,977
Probit	0.44	137.846	0.59	2,792	2,265
Quantal-linear	0.76	137.337	–0.25	**1,670**	**1,190**
Quantal-quadratic	0.26	138.466	0.96	3,135	2,598
Weibull	N/A	139.241	0.00002	2,022	1,196

[a]N/A = not applicable.

Source: NTP (1986).

Based on these results, the logistic, multistage, log-probit, probit, quantal-linear, and quantal-quadratic models showed adequate fit of the data. The multistage and quantal-linear models (shown in bold in the table) provided adequate goodness-of-fit *p* values and the lowest AIC values. Since both models provided the same data fit, the BMDs estimated from these models are identical. For follicular cell hyperplasia in the thyroid of male mice, the BMD$_{10}$ is 1,670 mg/kg-day and the BMDL$_{10}$ is 1,190 mg/kg-day.

APPENDIX C: BENCHMARK DOSE ANALYSIS OF CANCER ENDPOINTS

All the potential cancer endpoints in the rat and mouse chronic studies (NTP, 1986) expressed as responses from all the animals treated were modeled, and BMD modeling results are summarized below. All the cancer endpoints are modeled with the cancer model in the BMDS, version 1.40b.

Neoplastic Nodules in the Liver of Male Rats

In the rat chronic study (NTP, 1986), there was a dose-dependent increase in the incidences of neoplastic nodules in the livers of male rats. The incidences of the lesion were 1/50, 7/50, and 15/49 for control, low dose, and high dose, respectively. The original oral doses were 0, 1,120, and 2,240 mg/kg-day, and the corresponding HEDs are 0, 305.1, and 608.3 mg/kg-day, respectively. These incidence data on neoplastic nodules in male rats were modeled by using the multistage model as recommended for a tumorigenic endpoint, and the modeling results are summarized in Table C-1.

Table C-1. Summary of BMD modeling results for increase in neoplastic nodules in the liver of male rats

Model	Goodness-of-fit *p* value	AIC	$ED_{12.2}$	$LED_{12.2}$
Multistage	0.58	114.935	**250**	**174**

Source: NTP (1986).

The low-dose group resulted in an incidence of 7/50, which corresponds to 12.2% extra risk. Therefore, the cancer ED at an extra risk of 12.2% was estimated to be 250 mg/kg-day, and the corresponding LED is 174 mg/kg-day. The slope factor at the 12.2% extra risk is 0.0007 per mg/kg-day.

Neoplastic nodules in the liver of male rats (NTP, 1986)
BMR=12.2% extra risk

```
 ======================================================================
              Cancer Model. (Version: 1.2;  Date: 10/20/2005)
              Input Data File: C:\BMDS140B\UNSAVED1.(d)
              Gnuplot Plotting File:  C:\BMDS140B\UNSAVED1.plt
                                                   Thu Dec 01 00:38:02 2005
 ======================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:
P[response] = background + (1-background)*[1-EXP(-beta1*dose^1)]
The parameter betas are restricted to be positive
Dependent variable = response
Independent variable = dose

Total number of observations = 3
Total number of records with missing values = 0
Total number of parameters in model = 2
Total number of specified parameters = 0
Degree of polynomial = 1

Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

Default Initial Parameter Values
Background  =      0.0063916
Beta(1)     =      0.000566746

Asymptotic Correlation Matrix of Parameter Estimates
            Background  Beta(1)
Background  1           -0.73
Beta(1)     -0.73       1

Parameter Estimates
                                               95.0% Wald Confidence Interval
 Variable        Estimate        Std. Err        Lower Conf.     Upper Conf.
                                                 Limit           Limit
 Background      0.0190343       0.127925        -0.231695       0.269764
 Beta(1)         0.000520805     0.000351251     -0.000167635    0.00120924


Analysis of Deviance Table
 Model           Log(likelihood)     # Param's   Deviance   Test        P-value
                                                            d.f.
 Full model      -55.3119            3
 Fitted model    -55.4674            2           0.311055   1          0.577
 Reduced model   -63.9318            1           17.2399    2
                                                                       0.0001805

AIC:         114.935
```

```
Goodness of Fit
                                                Scaled
 Dose          Est._Prob     Expected     Observed      Size          Residual
 0.0000        0.0190        0.933        1             49            0.070
 305.1000      0.1632        8.158        7             50            -0.443
 608.3000      0.2854        13.984       15            49            0.321

 Chi^2 = 0.30      d.f. = 1        P-value = 0.5811

Benchmark Dose Computation
Specified effect        =     0.122
Risk Type          =     Extra risk
Confidence level   =     0.95

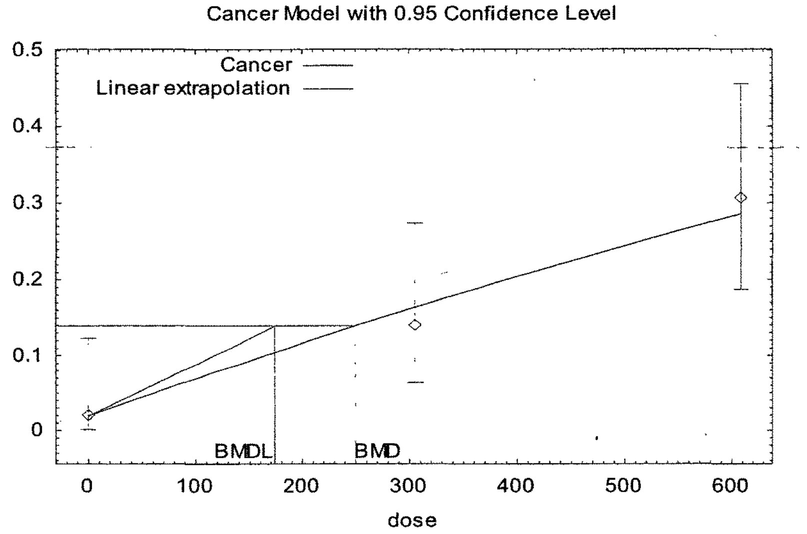
BMD          =      249.822

BMDL         =      173.541

BMDU          =     401.462

Taken together, (173.541, 401.462) is a 90% two-sided confidence interval for
the BMD

Cancer Slope Factor =    0.000703004
```



00:38 12/01 2005

Neoplastic Nodules or Carcinomas (Combined) in the Liver of Male Rats

The data (2/50, 8/50, and 15/49 for control, low dose, and high dose, respectively) on neoplastic nodules or carcinomas (combined) in the liver of male rats treated with decaBDE (NTP, 1986) were also modeled with BMDS. The modeling results are summarized in Table C-2.

Table C-2. Summary of BMD modeling results for increases in neoplastic nodules or carcinomas (combined) in the liver of male rats

Model	**Goodness-of-fit *p* value**	**AIC**	**$ED_{12.4}$**	**$LED_{12.4}$**
Multistage	0.71	125.18	**263**	**178**

Source: NTP (1986).

The low-dose group resulted in an incidence of 8/50, which corresponds to 12.4% extra risk. Therefore, the cancer ED at an extra risk of 12.4% was estimated to be 263 mg/kg-day, and the corresponding LED is 178 mg/kg-day. The slope factor at the 12.4% extra risk is 0.0007 per mg/kg-day.

Neoplastic Nodules or Carcinomas (Combined) in the Liver of Male Rats (NTP, 1986)
BMR=12.4% extra risk

```
 ====================================================================
              Cancer Model. (Version: 1.2;  Date: 10/20/2005)
              Input Data File: C:\BMDS140B\UNSAVED1.(d)
              Gnuplot Plotting File:  C:\BMDS140B\UNSAVED1.plt
                                                 Thu Dec 01 00:51:35 2005
 ====================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:
P[response] = background + (1-background)*[1-EXP(-beta1*dose^1)]
The parameter betas are restricted to be positive
Dependent variable = response
Independent variable = dose

Total number of observations = 3
Total number of records with missing values = 0
Total number of parameters in model = 2
Total number of specified parameters = 0
Degree of polynomial = 1

Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

Default Initial Parameter Values
Background  =      0.0312973
Beta(1)     =      0.00053218

Asymptotic Correlation Matrix of Parameter Estimates
            Background  Beta(1)
~~Background~~                ~~-0.73~~
Beta(1)     -0.73       1

Parameter Estimates
                                 95.0% Wald Confidence Interval
 Variable      Estimate      Std. Err.     Lower Conf. Limit  Upper Conf.
                                                              Limit
 Background    0.039023      0.127636      -0.21114           0.289186
 Beta(1)       0.000503605   0.000358293   -0.000198637       0.00120585

Analysis of Deviance Table
 Model         Log(likelihoo   #          Deviance     Test d.f.     P-value
               d)             Param's
 Full model    -60.5216        3
 Fitted        -60.5898        2          0.136394     1             0.7119
 model
 Reduced       -67.2168        1          13.3904      2              0.001237
 model

           AIC:          125.18
```

```
Goodness of Fit
                                                            Scaled
 Dose           Est._Prob.   Expected      Observed      Size          Residual
 0.0000         0.0390       1.912         2             49            0.065
 305.1000       0.1759       8.795         8             50            -0.295
 608.3000       0.2926       14.337        15            49            0.208

Chi^2 = 0.13      d.f. = 1        P-value = 0.7136

Benchmark Dose Computation
Specified effect        =     0.124
Risk Type          =     Extra risk
Confidence level  =      0.95

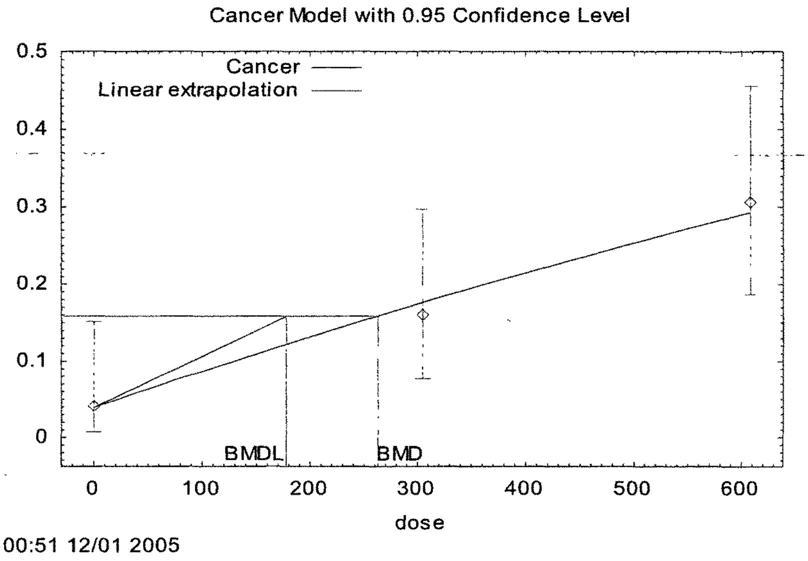
BMD         =      262.883

BMDL        =      177.57

BMDU        =       464.193

Taken together, (177.57 , 464.193) is a 90% two-sided confidence interval for
the BMD

Cancer Slope Factor =    0.000698317
```



Neoplastic Nodules in the Liver of Female Rats

In the rat chronic study (NTP, 1986), there was also a dose-dependent increase in the incidences of neoplastic nodules in the livers of female rats. The incidences of the lesion were 1/50, 3/49, and 9/50 for control, low dose, and high dose, respectively. The original oral doses were 0, 1,200, and 2,550 mg/kg-day, and the corresponding HEDs are 0, 292.2, and 618.4 mg/kg-day, respectively. The modeling results are summarized in Table C-3.

Table C-3. Summary of BMD modeling results for increases in neoplastic nodules in the liver of female rats

Model	**Goodness-of-fit *p* value**	**AIC**	**ED$_{4.2}$**	**LED$_{4.2}$**
Multistage	0.44	84.15	**171**	**103**

Source: NTP (1986).

The low-dose group resulted in an incidence of 3/49, which corresponds to 4.2% extra risk. Therefore, the cancer ED at an extra risk of 4.2% was estimated to be 171 mg/kg-day, and the corresponding LED is 103 mg/kg-day. The slope factor at the 4.2% extra risk is 0.0004 per mg/kg-day.

Neoplastic Nodules in the Liver of Female Rats (NTP, 1986)
BMR=4.2% extra risk

```
 ====================================================================
              Cancer Model. (Version: 1.2;  Date: 10/20/2005)
              Input Data File: C:\BMDS140B\UNSAVED1.(d)
              Gnuplot Plotting File:  C:\BMDS140B\UNSAVED1.plt
                                                  Thu Dec 01 01:12:25 2005
 ====================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:
P[response] = background + (1-background)*[1-EXP(-beta1*dose^1)]
The parameter betas are restricted to be positive
Dependent variable = response
Independent variable = dose

Total number of observations = 3
Total number of records with missing values = 0
Total number of parameters in model = 2
Total number of specified parameters = 0
Degree of polynomial = 1

Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

Default Initial Parameter Values
Background  =     0.00569581
Beta(1)     =     0.000290683

Asymptotic Correlation Matrix of Parameter Estimates
            Background  Beta(1)
Background  1           -0.73
Beta(1)     -0.73       1

Parameter Estimates
                                                       95.0% Wald
Confidence Interval
 Variable      Estimate      Std. Err.     Lower Conf. Limit  Upper Conf.
                                                              Limit
 Background    0.0173602     0.122542      -0.222817          0.257538
 Beta(1)                     0.000317551   -0.000371802        0.000872976
              0.000250587

                               Analysis of Deviance Table
 Model            Log(likelihood  #           Deviance    Test        P-value
                  )               Param's                 d.f.
 Full model       -39.7575        3
 Fitted model     -40.074         2           0.633004    1             0.4263
 Reduced model    -44.1226        1           8.73022     2           0.01271

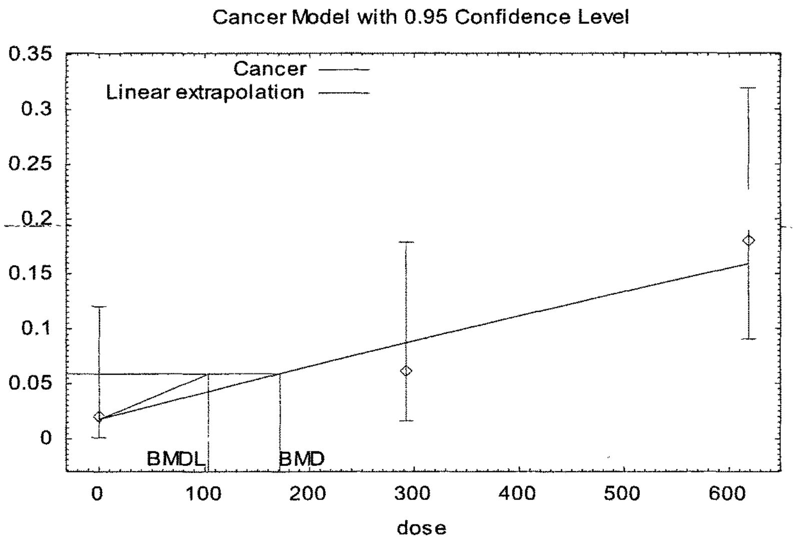
          AIC:           84.148
```

```
Goodness of Fit
                                             Scaled
 Dose          Est._Prob.    Expected     Observed       Size            Residual
 0.0000        0.0174        0.868        1              50              0.143
 292.2000      0.0867        4.250        3              49              -0.635
 618.4000      0.1584        7.921        9              50              0.418

 Chi^2 = 0.60      d.f. = 1        P-value = 0.4394

Benchmark Dose Computation
Specified effect  =      0.042
Risk Type         =      Extra risk
Confidence level  =      0.95
BMD               =      171.228
BMDL              =      103.205
BMDU              =      388.232

Taken together, (103.205, 388.232) is a 90% two-sided confidence interval for
the BMD
Cancer Slope Factor =    0.000406959
```



01:12 12/01 2005

Neoplastic Nodules and Carcinomas (Combined) in the Liver of Female Rats

The data (1/50, 5/49, and 9/50 for control, low dose, and high dose, respectively) on neoplastic nodules or carcinomas (combined) in the liver of female rats treated with decaBDE (NTP, 1986) were also modeled. The original oral doses were 0, 1,200, and 2,550 mg/kg-day, and the corresponding HEDs are 0, 292.2, and 618.4 mg/kg-day, respectively. The modeling results are summarized in Table C-4.

Table C-4. Summary of BMD modeling results for increases in neoplastic nodules and carcinomas (combined) in the liver of female rats

Model	Goodness-of-fit *p* value	AIC	$ED_{8.4}$	$LED_{8.4}$
Multistage	0.96	93.24	**301**	**186**

Source: NTP (1986).

The low-dose group resulted in an incidence of 5/49, which corresponds to 8.4% extra risk. Therefore, the cancer ED at an extra risk of 8.4% was estimated to be 301 mg/kg-day, and the corresponding LED is 186 mg/kg-day. The slope factor at the 8.4% extra risk is 0.0005 per mg/kg-day.

Neoplastic Nodules and Carcinomas (Combined) in the Liver of Female Rats (NTP, 1986)
BMR=8.4% extra risk

```
 ====================================================================
              Cancer Model. (Version: 1.2;  Date: 10/20/2005)
              Input Data File: C:\BMDS140B\UNSAVED1.(d)
              Gnuplot Plotting File:  C:\BMDS140B\UNSAVED1.plt
                                                  Thu Dec 01 01:23:38 2005
 ====================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:
P[response] = background + (1-background)*[1-EXP(-beta1*dose^1)]
The parameter betas are restricted to be positive
Dependent variable = response
Independent variable = dose

Total number of observations = 3
Total number of records with missing values = 0
Total number of parameters in model = 2
Total number of specified parameters = 0
Degree of polynomial = 1

Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

Default Initial Parameter Values
Background  =     0.0211024
Beta(1)     =     0.000288051

Asymptotic Correlation Matrix of Parameter Estimates

            Background      Beta(1)
Background  1            -0.75
Beta(1)     -0.75        1

Parameter Estimates
                                 95.0% Wald Confidence Interval
 Variable      Estimate      Std. Err.     Lower Conf. Limit   Upper Conf.
                                                               Limit
 Background    0.0202022     0.128079      -0.230828           0.271232
 Beta(1)       0.000291122   0.000344031   -0.000383167        0.00096541

                          Analysis of Deviance Table
 Model          Log(likelihood)    # Param's  Deviance     Test      P-value
                                                           d.f.
 Full model     -44.6193            3
 Fitted model   -44.6208            2          0.0030289    1         0.9561
                                               1
 Reduced        -48.6567            1          8.07484      2         0.01764
 model
          AIC:          93.2416
```

```
Goodness of Fit
                                                     Scaled
 Dose          Est._Prob.    Expected     Observed      Size          Residual
 0.0000        0.0202        1.010        1             50            -0.010
 292.2000      0.1001        4.905        5             49            0.045
 618.4000      0.1816        9.081        9             50            -0.030

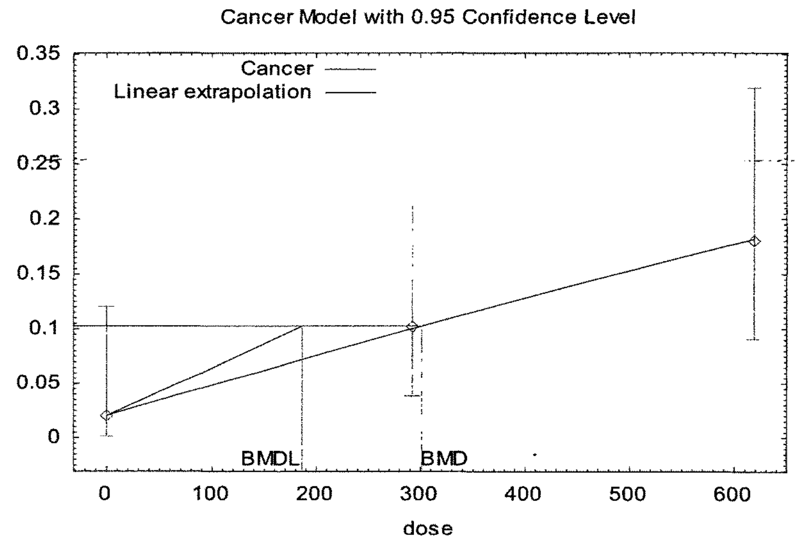

Chi^2 = 0.00       d.f. = 1         P-value = 0.9560

Benchmark Dose Computation
Specified effect  =     0.084
Risk Type         =     Extra risk
Confidence level  =     0.95

BMD         =     301.382
BMDL        =     186.131
BMDU         =     676.695

Taken together, (186.131, 676.695) is a 90% two-sided confidence interval for
the BMD

Cancer Slope Factor =    0.000451296
```



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Thyroid Follicular Cell Hyperplasia in Male Mice

In the mouse chronic study (NTP, 1986), there were slight increases in follicular cell adenomas or carcinomas (combined) accompanied by significant increase in follicular cell hyperplasia in male mice. Because the follicular cell hyperplasia is considered a stage of the thyroid cell carcinogenic process, this endpoint was also modeled as a cancer endpoint. Therefore, the data (2/50, 10/50, and 19/50 for control, low dose, and high dose, respectively) on follicular cell hyperplasia in the thyroid of male mice treated with decaBDE (NTP, 1986) were modeled. The original oral doses were 0, 3,200, and 6,650 mg/kg-day, and the corresponding HEDs are 0, 486.5, and 1,008.6 mg/kg-day, respectively. The modeling results are summarized in Table C-5.

Table C-5. Summary of BMD modeling results for increases in thyroid follicular cell hyperplasia as a key event of thyroid tumor in male mice

Model	Goodness-of-fit *p* value	AIC	$ED_{16.7}$	$LED_{16.7}$
Multistage	0.75	137.34	**440**	**313**

Source: NTP (1986).

The low-dose group resulted in an incidence of 10/50, which corresponds to 16.7% extra ~~risk. Therefore, the cancer ED at an extra risk of 16.7% was estimated to be 440 mg/kg-day, and~~ the corresponding LED is 313 mg/kg-day. The slope factor at the 16.7% extra risk is 0.0005 per mg/kg-day.

Thyroid Follicular Cell Hyperplasia in Male Mice (NTP, 1986)
BMD:16.7%

```
 ====================================================================
              Cancer Model. (Version: 1.2;  Date: 10/20/2005)
              Input Data File: C:\BMDS140B\UNSAVED1.(d)
              Gnuplot Plotting File:  C:\BMDS140B\UNSAVED1.plt
                                                   Thu Dec 01 01:32:16 2005
 ====================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:
P[response] = background + (1-background)*[1-EXP(-beta1*dose^1)]
The parameter betas are restricted to be positive

Dependent variable = response
Independent variable = dose
Total number of observations = 3
Total number of records with missing values = 0
Total number of parameters in model = 2
Total number of specified parameters = 0
Degree of polynomial = 1

Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

Default Initial Parameter Values
Background    =    0.0304923
Beta(1)       =    0.000434152

Asymptotic Correlation Matrix of Parameter Estimates

            Background  Beta(1)
Background  1           -0.72
Beta(1)     -0.72       1

Parameter Estimates
                        95.0% Wald Confidence Interval
 Variable      Estimate      Std. Err.     Lower Conf. Limit   Upper Conf.
                                                               Limit
 Background    0.0386341     0.126668      -0.209631            0.2869
 Beta(1)                     0.000222182   -1.97658e-005       0.00085117
               0.000415702

                          Analysis of Deviance Table
 Model           Log(likelihood)    # Param's  Deviance     Test      P-value
                                                            d.f.
 Full model      -66.6205           3
 Fitted model    -66.6699           2          0.0987661    1         0.7533
 Reduced         -76.426            1          19.6109      2         <.0001
 model
           AIC:            137.34
```

```
Goodness of Fit
                                                               Scaled
 Dose          Est._Prob.    Expected      Observed      Size          Residual
 0.0000        0.0386        1.932         2             50            0.050
 486.5000      0.2147        10.733        10            50            -0.252
 1008.6000     0.3679        18.394        19            50            0.178

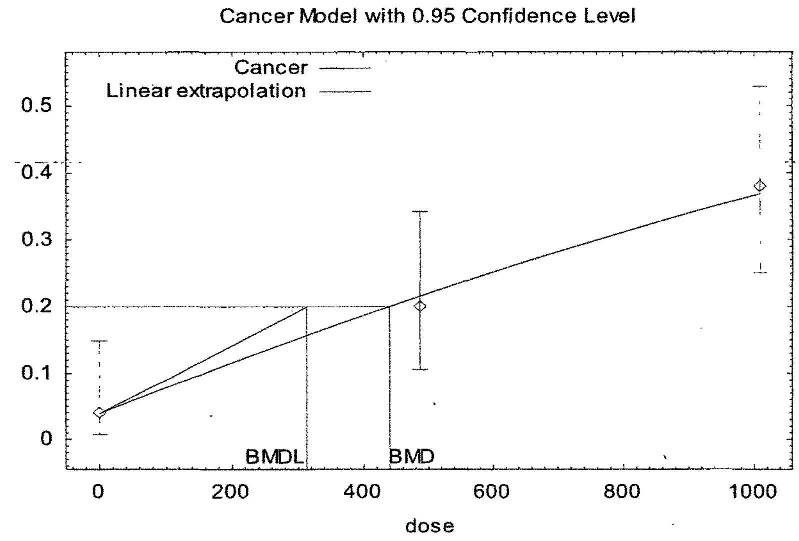
Chi^2 = 0.10      d.f. = 1        P-value = 0.7544

Benchmark Dose Computation
Specified effect  =      0.167
Risk Type         =      Extra risk
Confidence level  =      0.95

BMD          =      439.549
BMDL         =      313.299
BMDU         =      685.676

Taken together, (313.299, 685.676) is a 90% two-sided confidence interval for
the BMD

Cancer Slope Factor =    0.000533037
```



01:32 12/01 2005

Combined Incidence of Hepatocellular Adenomas or Carcinomas in Male Mice

In the mouse chronic study (NTP, 1986), there were significant increases in combined hepatocellular adenomas or carcinomas in male mice. Therefore, the data (8/50, 22/50, and 18/50 for control, low dose, and high dose, respectively) on combined hepatocellular adenomas or carcinomas of male mice treated with decaBDE (NTP, 1986) were modeled. The original oral doses were 0, 3200, and 6650 mg/kg-day, and the corresponding HEDs are 0, 486.5, and 1008.6 mg/kg-day, respectively. The modeling results are summarized in Table C-6.

Table C-6. Summary of BMD modeling results for increases in combined hepatocellular adenomas or carcinomas in male mice

Model	Goodness-of-fit p value	AIC	$ED_{33.3}$	$LED_{33.3}$
Multistage	0.03	186.5	**1154**	**680**

Source: NTP (1986).

The low-dose group resulted in an incidence of 22/50, which corresponds to 33.3% extra risk. Therefore, the cancer ED at an extra risk of 33.3% was estimated to be 1,154 mg/kg-day, and the corresponding LED is 680 mg/kg-day. The slope factor at the 33.3% extra risk is 0.0005 per mg/kg-day.

Combined Incidence of Hepatocellular Adenomas or Carcinomas in Male Mice (NTP, 1986)
BMR=33.3% extra risk

```
 ====================================================================
              Cancer Model. (Version: 1.2;  Date: 10/20/2005)
              Input Data File: C:\BMDS140B\UNSAVED1.(d)
              Gnuplot Plotting File:  C:\BMDS140B\UNSAVED1.plt
                                                  Thu Dec 01 01:47:16 2005
 ====================================================================
 BMDS MODEL RUN
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
The form of the probability function is:

P[response] = background + (1-background)*[1-EXP(-beta1*dose^1)]

The parameter betas are restricted to be positive

Dependent variable = response
Independent variable = dose

Total number of observations = 3
Total number of records with missing values = 0
Total number of parameters in model = 2
Total number of specified parameters = 0
Degree of polynomial = 1

Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

                  Default Initial Parameter Values
                     Background =      0.235837
                        Beta(1) =   0.000263218


Asymptotic Correlation Matrix of Parameter Estimates

            Background  Beta(1)
Background  1           -0.77
Beta(1)     -0.77       1

Parameter Estimates
                        95.0% Wald Confidence Interval
 Variable      Estimate     Std. Err.    Lower Conf. Limit   Upper Conf.
                                                             Limit
 Background    0.19695      0.125592     -0.0492049          0.443105
 Beta(1)       0.000350822   0.00026836  -0.000175153        0.000876797

                          Analysis of Deviance Table
 Model           Log(likelihood)   # Param's  Deviance      Test      P-value
                                                            d.f.
 Full model      -88.9509           3
 Fitted model    -91.2692           2          4.63657      1         0.0313
 Reduced                 -94.0304   1          10.159       2         0.006223
 model


Goodness of Fit
                                   Scaled
 Dose         Est._Prob.   Expected     Observed     Size         Residual
 0.0000       0.1970       9.848        8            50           -0.657
 486.5000     0.3230       16.148       22           50           1.770
 1008.6000    0.4363       21.813       18           50           -1.087
```

```
Chi^2 = 4.75      d.f. = 1        P-value = 0.0293

Benchmark Dose Computation
Specified effect  =     0.333
Risk Type         =     Extra risk
Confidence level  =     0.95

BMD         =     1154.33
BMDL        =     680.241
BMDU        =     3796.73

Taken together, (680.241, 3796.73) is a 90% two-sided confidence interval for
the BMD

Cancer Slope Factor =   0.000489532
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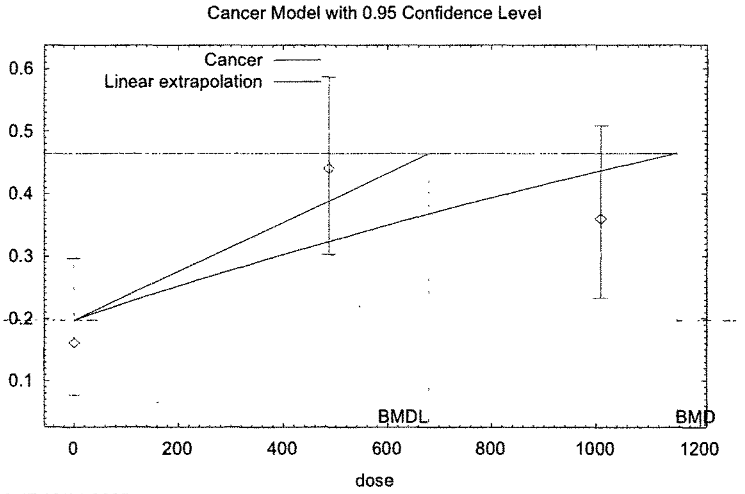

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OFFICE OF INSPECTOR GENERAL

Catalyst for Improving the Environment

Ombudsman Report

Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia

Report 2005-P-00022

September 26, 2005

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Abbreviations

ATSDR	Agency for Toxic Substances and Disease Registry
CLE	Cod Liver Extract
Corps	U. S. Army Corps of Engineers
DDE	Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
DNA	Deoxyribonucleic Acid
EPA	U. S. Environmental Protection Agency
EUSES	European Union System for the Evaluation of Substances
GA/DNR	Georgia Department of Natural Resources
GC/ECD	Gas Chromatograph/Electron Capture Detector
GC/NIMS	Gas Chromatograph/Negative Ion Mass Spectroscopy
GEPD	Georgia Environmental Protection Division
HCH	Hexachlorocyclohexane
IRIS	Integrated Risk Information System
~~MATT~~	~~Monitoring, Analysis, and Toxicity of Toxaphene in Marine Foodstuff~~
MNA	Monitored Natural Attenuation
NIMS	Negative Ion Mass Spectroscopy
OIG	Office of Inspector General
OSWER	Office of Solid Waste and Emergency Response
PCB	Polychlorinated Biphenyls
ppb	Parts Per Billion
ppt	Parts Per Trillion
RPM	Remedial Project Manager
SESD	Science and Ecosystem Support Division
TCDD	Tetrachlorodibenzo-p-dioxin
TDI	Tolerable Daily Intake

Cover photo: Aerial view of the Hercules 009 Landfill, which is in the center and left-center of this photograph, provided by Hercules Incorporated.

U.S. Environmental Protection Agency
Office of Inspector General

2005-P-00022
September 26, 2005

At a Glance

Catalyst for Improving the Environment

Why We Did This Review

The Glynn Environmental Coalition, a nonprofit community organization whose goal is to have a safe and healthy place to live and raise a family, brought several concerns to the Ombudsman's attention regarding the Hercules 009 Landfill site near Brunswick, Georgia, in EPA Region 4.

Background

Between 1975 and 1980, Hercules Incorporated operated the Hercules 009 Landfill to dispose of waste material from producing toxaphene, an agricultural pesticide. The site became part of EPA's Superfund program in 1984. Construction on the cleanup was completed in 1999, but some contaminants remained at the site, so every 5 years the site must be reviewed to ensure that the cleanup is functioning as intended and it does not adversely affect human health and the environment.

For further information, contact our Office of Congressional and Public Liaison at (202) 566-2391.

To view the full report and addendum, click on the following links:

www.epa.gov/oig/reports/2005/20050926-2005-P-00022.pdf

www.epa.gov/oig/reports/2005/20050926-2005-P-00022A.pdf

Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia

What We Found

The testing method that EPA uses to monitor for the presence of toxaphene in groundwater is inadequate. Toxaphene degrades over time, changing into other products (toxaphene breakdown products). EPA's testing method does not identify and measure the amount of toxaphene that has degraded, only toxaphene that has not degraded.

The available toxicity data on the toxaphene breakdown products are not specific as to what constitutes a safe, acceptable level of exposure. Because toxaphene breakdown products may pose a risk to human health, they should be monitored. A different analytical method, one that monitors toxaphene breakdown products, should be used rather than the conventional EPA method.

EPA's report on the 5-year review of the Hercules 009 Landfill is over a year late, because

- Region 4 was gathering additional data to reduce uncertainty about how much toxaphene was present in the groundwater.
- The U.S. Army Corps of Engineers took longer to prepare the first draft report than expected.
- The EPA manager for the site changed twice during the review period.
- EPA and others made extensive comments on the draft reports.

What We Recommend

We recommend that EPA Region 4:

- use an analytical method that monitors both toxaphene and its breakdown products in the groundwater at the Hercules 009 Landfill and take appropriate action if toxaphene breakdown products are found.
- issue the report on the Hercules 009 Landfill 5-year review.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
INSPECTOR GENERAL

September 26, 2005

MEMORANDUM

SUBJECT: Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia
Report No. 2005-P-00022

FROM: Paul D. McKechnie /s/
Acting Ombudsman
Office of Congressional and Public Liaison

TO: J. I. Palmer, Jr.
Regional Administrator, Region 4

This is our final report on our review of complaints regarding the Hercules 009 Landfill Superfund site conducted by the Office of Inspector General (OIG) of the U.S. Environmental Protection Agency (EPA). This report contains findings that describe the problems the OIG identified and corrective action the OIG recommends. It represents the opinion of the OIG and findings contained in this report do not necessarily represent the final EPA position. Final determinations on matters in this report will be made by EPA managers in accordance with established resolution procedures.

Action Required

In accordance with EPA Manual 2750, you are required to provide a written response to this report within 90 calendar days of the date of this report. You should include a corrective actions plan for agreed upon actions, including milestone dates. We have no objections to the further release of this report to the public. For your convenience, this report will be available at http://www.epa.gov/oig/publications.htm.

If you or your staff have any questions regarding this report, please contact me at 617-918-1471 or Christine Baughman, the Project Manager, at 202-566-2902.

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Chapter 1

Introduction

Objectives

The Glynn Environmental Coalition, a nonprofit community organization whose goal is to have a safe and healthy place to live and raise a family, brought some issues regarding the Hercules 009 Landfill, Brunswick, Georgia, to the attention of the Ombudsman at the U.S. Environmental Protection Agency's (EPA) Office of Inspector General (OIG). (The OIG Ombudsman reviews and reports on public concerns regarding EPA activities, including Superfund.)

As a result, the OIG conducted a review of the issues to determine:

-- If human health at the Hercules 009 Landfill Superfund site and/or surrounding area were threatened because the analytical method used to test for the pollutant toxaphene underestimated the amount of toxaphene breakdown products.

-- If the February 2004 draft report on the 5-year review, which addressed the above and various other issues, was issued in a timely manner by EPA.

Site Information

Hercules Incorporated began producing toxaphene, an agricultural pesticide, in 1948 and continued production through 1980. Toxaphene was one of the most heavily used insecticides in the United States until 1982, when EPA cancelled the registrations for most uses; all uses were banned in 1990. A registration is a license allowing a pesticide product to be sold and distributed for specific uses in accordance with specific use instructions, precautions, and other terms and conditions. Between 1975 and 1980, Hercules Incorporated operated the Hercules 009 Landfill under a permit issued by the Georgia Environmental Protection Division (GEPD). The permit allowed the Brunswick, Georgia, Hercules plant to dispose of waste water sludge left over from having produced toxaphene. Part of the Hercules 009 Landfill was also used for disposing empty toxaphene drums and toxaphene-contaminated glassware, rubble, and trash. The GEPD monitored the Hercules 009 Landfill while it operated.

The Hercules 009 Landfill is located in the eastern portion of Glynn County, Georgia, near the City of Brunswick. The site is a 16.5 acre property, although the landfill occupies only about 7 acres on the north end of the property. It is bordered by Georgia State Highway 25 (Spur 25) on the west; an automobile dealership on the north; a pine forest on the east; and several homes, a church, a school, and a strip shopping center on the south/southeast. A shopping mall built in 1985, a bank, and a restaurant are located approximately 1000 feet north of the landfill. In the forested area in the southeastern part of the site, outside of the protectively capped area, is a storage shed near a small pond. The property is surrounded by a fence with locked gates.

EPA added the Hercules 009 Landfill to the Superfund National Priority List in 1984. In December 1992, EPA completed an interim cleanup action at the site. As part of the interim action, private wells immediately down gradient of the landfill were replaced by the municipal water system. Further site cleanup action, known as remedial action, began at the site in June 1998. The remedial action involved stabilizing the site and constructing a landfill cover, which was then covered with clean fill material that was graded to promote adequate drainage, and seeded with grass. Although active cleanup of the groundwater was not included, groundwater monitoring was required to assess (1) any movement of contamination through groundwater and (2) reduction of contaminants through natural means, known as natural attenuation.

Background Information on Toxaphene

Unlike most organic environmental pollutants, toxaphene is not a single organic compound. As manufactured, the original toxaphene pesticide was a mixture of more than 200 closely related chlorinated organic compounds. This original toxaphene pesticide mixture is commonly known as "technical" toxaphene. Technical toxaphene consists mainly of polychlorinated bornanes with between six to nine chlorines attached. The term "congener" is used to refer to a single, structurally unique constituent of the mixture. In other words, at least 200 individual toxaphene congeners make up the original toxaphene pesticide mixture. Individual congeners are often given their own name, such as Hx-Sed and Hp-Sed. When the original toxaphene is released to the environment, it naturally breaks down or degrades. These breakdown products are a different mixture than the original toxaphene mixture, so it appears different to the testing instruments.

Scope and Methodology

The OIG began preliminary research on the site in late 2002 and completed work in April 2004. It started the field work on this review in June 2004 and completed it in January 2005.

We interviewed the present and two former remedial project managers (RPMs) from EPA Region 4 and other Region 4 officials, and reviewed site files. We also interviewed representatives of the U.S. Army Corps of Engineers (Corps) and the

Glynn Environmental Coalition. A representative of Hercules Incorporated provided the OIG team and Corps officials a tour of the site.

We interviewed representatives of EPA's Office of Research and Development and Office of Solid Waste and Emergency Response. The OIG team reviewed toxaphene testing protocols and about 50 journal articles on toxaphene toxicity and exposure issues. The team also obtained additional information from various State and Federal Internet sites.

On May 16, 2005, the OIG issued a draft report to EPA's Region 4 for review and comment. The Regional Administrator responded on June 29, 2005. This response, which included six attachments with detailed technical and legal comments, suggested alternative actions to address the matters discussed in the draft report. We provide a summary and general evaluation of the EPA comments and our response at the end of Chapter 2 and Chapter 3 of this report. We included the Regional Administrator's memorandum in Appendix B. The memorandum, together with the six attachments and other documents later provided by Region 4, are available as an addendum to this report. Appendix C is the OIG evaluation of the EPA response, including the review that Region 4 requested of their proposed interim strategy for risk assessment.

We performed our review in accordance with *Government Auditing Standards* issued by the Comptroller General of the United States. However, our review of management controls and compliance was limited to those related to this particular Superfund site.

The findings in this report are not binding in any enforcement proceedings brought by EPA or the Department of Justice under the Comprehensive Environmental Response, Compensation, and Liability Act to recover costs incurred not inconsistent with the National Contingency Plan.

Chapter 2

The Groundwater Should be Tested for Toxaphene Breakdown Products

EPA policy states that monitoring programs should identify any potentially toxic transformation products. Thus, the groundwater at the Hercules 009 Landfill site should be periodically tested for toxaphene and its toxic breakdown products. To determine if the groundwater is contaminated by toxaphene breakdown products, the EPA needs to use a new analytical method that specifically tests for these products. Until EPA knows whether the groundwater is contaminated by toxaphene breakdown products, it will be unable to definitively determine if the cleanup for the Hercules 009 Landfill protects human health. Appendix A contains a technical discussion of the matters addressed in this chapter.

Testing for Toxaphene Breakdown Products Is Needed

Part of the cleanup at the Hercules 009 Landfill site is monitored natural attenuation (MNA or natural attenuation). A natural attenuation remedy (or cleanup) is one in which environmental contamination remains on-site and is allowed to naturally decompose. For a natural attenuation cleanup to protect human health, the environmental contaminants cannot migrate off the site through, for example, the movement of contaminated groundwater. Therefore, contaminants known to be at the site, as well as any toxic chemicals resulting from the breakdown of those contaminants, should be periodically tested (i.e., monitored) in the groundwater. In the case of Hercules 009 Landfill, the surrounding groundwater is being periodically tested for the original toxaphene mixture put in the site between 1975 and 1980. However, this routine testing does not specifically look for, or definitively identify, individual breakdown products of toxaphene, i.e., the toxaphene breakdown products.

According to Superfund's guidance for monitored natural attenuation (OSWER—Office of Solid Waste and Emergency Response--Directive 9200.4-17P), EPA should look for the potential presence of toxic transformation products. Toxaphene breakdown products are a type of transformation product. Specifically, the guidance states:

> *The potential for creation of toxic transformation products is more likely to occur at non-petroleum release sites ... and should be evaluated to determine if implementation of a MNA [natural attenuation] remedy is appropriate and protective in the long term.*

Furthermore, the guidance states:

> *... all [MNA or natural attenuation] monitoring programs should be designed to accomplish the following: ... Identify any potentially toxic and/or mobile transformation products.*

In other words, EPA's guidance requires groundwater monitoring for breakdown products when the following two conditions are met: (1) the original contaminant is known to decompose and form breakdown product(s), and (2) these breakdown products are thought to be toxic and/or mobile in the groundwater. Since toxaphene is known to degrade in the environment and these breakdown products are thought to be toxic, EPA must evaluate the groundwater at the Hercules 009 Landfill site for toxaphene breakdown products.

EPA's Method Fails to Identify Toxaphene Breakdown Products in Groundwater

The EPA conventional analytical method (known as Method 8081) is currently used to monitor toxaphene in the groundwater at the Hercules 009 landfill site. EPA's method is a test procedure designed to look for the original, unaltered toxaphene mixture. However, microbes in the soil are known to decompose the original toxaphene mixture into just two major breakdown products (i.e., Hx-Sed and Hp-Sed) and several minor breakdown products. The original toxaphene ~~mixture and the two principal toxaphene breakdown products look completely~~ different to the analytical instruments. As a result, the groundwater monitoring data collected at the site, using EPA's method, only identified the original toxaphene mixture in the groundwater. The laboratory results from the EPA method clearly indicated that groundwater surrounding the site does not contain the original toxaphene mixture.

The groundwater surrounding the site could be contaminated with toxaphene breakdown products. Unfortunately, EPA's method does not look for, or specifically identify, toxaphene breakdown products. Therefore, the groundwater monitoring by EPA's method does not meet the Agency's requirement to monitor for toxaphene breakdown products, and the current groundwater monitoring data from the Hercules 009 Landfill site cannot be used to determine whether the groundwater could be contaminated by toxaphene breakdown products.

Using a Different Method Would Identify Breakdown Products

When the OIG looked at the groundwater monitoring data for evidence of toxaphene breakdown products, the OIG found some evidence suggesting that toxaphene breakdown products may be in the groundwater surrounding the Hercules 009 Landfill site. However, these groundwater monitoring data are insufficient to definitively determine the presence or absence of toxaphene breakdown products in the groundwater. Without such definitive data, any determination on the effectiveness of the cleanup remedy is inconclusive.

A new analytical method using Negative Ion Mass Spectroscopy (NIMS, or called the new method hereafter) should be used to test for toxaphene breakdown products in the groundwater. Academia and the European Union have successfully used the new method for at least 5 years to test for toxaphene breakdown products in the environment.

The new method provides definitive test results because the technique generates a mass spectrum for each compound in an environmental sample. A mass spectrum is analogous to a chemical "fingerprint." By comparing the "fingerprint" of an unknown compound in the Hercules 009 groundwater sample with the known "fingerprint" of the toxaphene breakdown products, a resulting match of the "fingerprints" would definitively identify the presence of toxaphene breakdown products.

On the other hand, if the "fingerprints" do not match, then the new technique would definitively determine that toxaphene breakdown products are not present in the groundwater. Therefore, the use of the new technique for groundwater monitoring at the Hercules 009 Landfill site provides the certainty needed to determine whether the groundwater is contaminated by toxaphene breakdown products. This information could then be used in the 5-year review to accurately determine the effectiveness of the Hercules 009 Landfill cleanup remedy.

Region 4 Is Concerned about Using the New Method

Region 4 officials are concerned about using the new (or NIMS) method to test groundwater at the Hercules 009 Landfill because the method is not approved by EPA. When using environmental data for public health decisions, Region 4 prefers to use approved methods that have been validated by several laboratories. The EPA conventional method (Method 8081) was validated. Consequently, EPA knows the results will be accurate when Method 8081 is used to test for the original toxaphene mixture.

The OIG agrees that using an EPA-approved method is better than a method not approved by EPA. However, EPA has no approved method to identify toxaphene breakdown products. Thus, to decide if the cleanup is effective, Region 4 must use an unapproved method to obtain the necessary information on the presence or absence of toxaphene breakdown products.

Under EPA's hazardous waste program, unapproved methods may be used. The conventional method (Method 8081) is in the EPA publication SW-846, entitled *Test Methods for Evaluating Solid Waste, Physical/Chemical Methods.* It is the official collection of analytical and sampling methods that EPA has evaluated and approved for use in complying with the hazardous waste regulations. SW-846 functions primarily as a guidance document setting forth acceptable, although not required, methods for the regulated and regulatory communities to use. The related EPA program office continually reviews advances in analytical instruments and techniques, and periodically updates SW-846 to improve method performance and cost effectiveness. However, the methods are guidance and not mandatory:

> *Except where explicitly specified in a regulation, the use of SW-846 methods is not mandatory in response to Federal testing requirements. ... The Agency does not intend to restrict the use of new analytical techniques. Advances in technologies applicable to the sampling and analysis of environmental media and hazardous wastes outpace the ability of the Agency to promulgate revisions to this manual. ... In summary, the methods included here provide guidance to the analyst and the regulated community in making judgements [sic] necessary to generate data that meet the data quality objectives for the intended use of the results.*

The EPA Region 4 laboratory has the capability to run the new (NIMS) method. However, the Region 4 laboratory personnel will need to learn the procedures, show they work, and practice using them before actually testing groundwater samples from the Hercules 009 Landfill. Thus, implementing the new method will take more laboratory resources, but is needed to obtain the necessary information to decide if the cleanup is effective.

Recommendations

We recommend that the Regional Administrator, Region 4:

2.1 Use negative ion mass spectroscopy to definitively determine if toxaphene breakdown products are present in the surrounding groundwater at the Hercules 009 Landfill site, and (if so) in what amounts.

2.2 If toxaphene breakdown products are found in the groundwater, assess the resulting risk to human health and take appropriate action.

Agency Comments and OIG Evaluation

The Agency generally agreed with our recommendations in Chapter 2. Under a voluntary interim action, Hercules Incorporated had samples collected in March 2005 from the monitoring wells at the Hercules 009 Landfill analyzed. These samples were analyzed using the negative ion mass spectrometry as well as EPA method 8081. The results of these analyses, which were provided as Attachment 1 to the Region 4 response and are in the Addendum to this report, were less than the maximum contaminant level for toxaphene in drinking water (i.e., 3 micrograms per liter). Region 4 later provided results of analytical testing they had performed using EPA method 8081. Their results showed significantly more toxaphene in one well (N-11) at the site. These results are in the Addendum to this report.

The OIG evaluated these analyses of the groundwater. As discussed in Appendix C, the quality control does not adequately show that the substances to be measured were not destroyed when the samples were prepared. We believe this situation confirms the need for EPA to develop and validate a standard NIMS method for analyzing samples for toxaphene breakdown products.

Region 4 confirmed they have the instrumentation necessary to perform the NIMS procedure, but additional resources would be needed to implement the method in the Region 4 laboratory. They would be willing to help validate the method.

> *Region 4's laboratory is willing to participate in a multi-laboratory method validation study for toxaphene congeners in environmental samples. However, since the Agency as a whole would obviously benefit from a validated NIMS method for toxaphene congeners, we believe that a multi-laboratory method validation study should be initiated at the program level by the Office of Solid Waste and Emergency Response. A validated method will serve both the regulated community and the Agency by assuring that analytical data produced by the method are defensible, of known quality, and suitable for risk assessment decision making.*

Region 4 proposed two interim strategies to assess the risk to human health posed by the toxaphene breakdown products, which they called weathered toxaphene. The proposed strategy preferred by Region 4 uses toxicity criteria developed by Region 4 staff. It is based, in part, on the sole toxicological study of weathered toxaphene, which is the Monitoring, Analysis, and Toxicity of Toxaphene in Marine Foodstuff (a.k.a. MATT) from the European Union, but they identified several concerns about the study. Region 4 agreed that additional toxicity studies would be helpful in filling data gaps, and (in Attachment 2 to the Region 4 response) suggested several studies. Region 4 requested that the OIG assess the soundness and applicability of these criteria. The other strategy uses toxicity criterion for technical, or original, toxaphene.

We evaluated the proposed strategies, and believe the strategy using toxicity criteria for toxaphene is inappropriate because the toxicity of weathered toxaphene could be significantly different. The toxicity criterion developed by the Region 4 staff for weathered toxaphene is innovative in that Region 4 developed a reference dose for weathered toxaphene. A reference dose is the concentration of a chemical believed to cause health problems. Thus, to ensure no ill effects, people should not be exposed to more than the reference dose. According to a Region 4 toxicologist (in the updated Attachment 2 to the Region 4 response, which is in the Addendum to this report):

> *This use of the reference dose represents one of the first instances in which EPA has applied a threshold-type toxicity to a potentially carcinogenic chemical. This procedure is consistent with EPA's new cancer guidelines and with the goal of harmonization of cancer and non-cancer risk assessment.*

As discussed in more detail in Appendix C, because developing this reference dose is so innovative, it should be subjected to internal and external peer review before being applied. Given the problems in analyzing the groundwater from the Hercules 009 Landfill, the need for a risk assessment for this site has not yet been established.

Chapter 3

Reporting on the Cleanup's Effectiveness Was Not Timely

Every 5 years EPA must review the effectiveness of the Hercules 009 Landfill cleanup, determining whether the cleanup is operating as intended and still protects human health and the environment. EPA did not issue the report on the second 5-year review timely; though due in September 2003, it remains in draft form. The chief reason for delay was because Region 4 officials wanted to ensure the cleanup was effective.

The latest report draft, dated February 2004, concluded that the cleanup was operating as intended. We initially believed the report should be issued, concluding that the effectiveness of the cleanup cannot be determined because the EPA conventional toxaphene test method (Method 8081) cannot determine whether breakdown products are present in the groundwater. However, we now agree Region 4 can conclude the cleanup was operating as intended.

Reviews Must Occur Every 5 Years

According to Section 121(c) of the Comprehensive Environmental Response, Compensation, and Liability Act and related regulations, cleanup actions must be reviewed every 5 years when hazardous substances, pollutants, or contaminants remain at the site, as was the case with the Hercules 009 Landfill. According to EPA's June 2001 *Comprehensive Five-Year Review Guidance*, the purpose of the 5-year review was to evaluate, through data gathering and observation, how well the site's remedy is working. The technical evaluation should address the following three questions. We believe the answer to Question B would be affected if toxaphene breakdown products were found in the groundwater surrounding the Hercules 009 Landfill.

- Question A – Is the remedy operating as intended by the decision documents?
- Question B – Are the exposure assumptions, toxicity data, cleanup levels, and remedial action objectives used when the remedy was selected still valid?
- Question C – Has any other information come to light that could call into question if the remedy protects human health and the environment?

EPA issued the report on the first 5-year review in September 1998. Thus, according to Agency guidance, the next 5-year review was due in September 2003.

Second Report's Delay Was Chiefly to Ensure Cleanup Effectiveness

For the second review, the U.S. Army Corps of Engineers, or the Corps (while working for EPA) gathered information from July 2002 through December 2002. The Corps sent EPA the first draft 5-year review report in January 2003 and the most recent, complete draft in February 2004. As of January 2005, the report on the second 5-year review still had not been issued. It was delayed primarily because of Region 4's efforts to decide if the cleanup protects human health and the environment. Reaching such a decision was complicated by the issues addressed in Chapter 2. Delay resulted when EPA tried to resolve some of the technical concerns by re-evaluating some existing information and obtaining additional data.

In September 2003, the RPM (the Remedial Project Manager) asked the Region 4 groundwater expert to review the hydrological data for the Hercules 009 Landfill site and determine if the monitoring wells were properly located. In December 2003, this expert sent the RPM a groundwater flow map and a memorandum noting that the monitoring wells were properly located to evaluate the groundwater.

The 5-year review draft reports used groundwater monitoring data collected through November 2002. In June 2004, Hercules Incorporated performed another round of groundwater testing. Region 4's laboratory also analyzed samples from this round, but used a different option to measure the toxaphene. Another round of groundwater testing was performed in September 2004, with the Region 4 laboratory again analyzing the samples. The results of this round became available in November 2004.

Other factors delaying the report were the following:

- Corps officials acknowledged that due to staffing, data gathering, and other problems, they took 8 months to complete their fieldwork and submit the first draft report to EPA.
- The EPA official in charge of the site, the RPM, changed in April 2002 and again in March 2003. The Corps and current RPM believe that additional review time by new RPMs delayed the report.
- The Glynn Environmental Coalition submitted extensive comments on the February 2004 report draft. Several sources outside the Region were asked to submit responses, so the Region required additional time to collate and address responses.
- In January 2004, the Glynn Environmental Coalition requested a substantial amount of information, and the Region delayed the report to respond to the request.

- Once the Ombudsman notified Region 4 that we intended to review actions at the site, Region 4 staff said they intended to delay issuing the report on the 5-year review. They want to know what the Ombudsman's report will contain, so the reports do not conflict.

EPA Policy Requires the Reviewer to Make a Decision

According to EPA's June 2001 *Comprehensive Five-Year Review Guidance,* at the end of the technical analysis and evaluation phase of the 5-year review, the reviewer must make a decision about the cleanup's effectiveness and document this decision (or determination) in a report on the review. Based on the answers to the three technical questions, the reviewer may decide that the cleanup protects human health, will protect it once the cleanup is completed, will protect it in the short term, or will not protect it. The reviewer can also conclude that protection cannot be determined until further information is obtained. If a protection statement cannot be made, a time frame should be provided when such a statement will be made, through an addendum. If this is the case, the next 5-year review is due 5 years from the date that the report is signed, not from the signature date of the addendum.

Further Definite Information Is Needed

Between the first draft report of the 5-year review and the most recent one, the conclusion on the cleanup's effectiveness changed; we agree with the Corps' original conclusion that additional information is needed to responsibly make a determination. The protection determination proposed by the Corps in the January 2003 draft report stated that the cleanup action should be protective when the groundwater cleanup goals were reached. However, it also stated that the data being collected was not appropriate to determine if the cleanup is functioning. The Corps believed the data were not appropriate based on three main factors: toxicity of toxaphene breakdown products, appropriateness of the selected groundwater sampling methodology, and appropriateness of the analytical method used to test the groundwater.

In the February 2004 draft, the first sentence of the determination remained the same, i.e., the cleanup actions at the site are expected to be protective upon attainment of groundwater cleanup goals. However, the subsequent sentences in the first paragraph of the determination were deleted, including the caveat about the data:

> *The review of documents, [applicable and relevant and appropriate requirements], risk assumptions and analytical data and site inspections indicate that the data being collected is not appropriate to determine if the remedy [cleanup] is functioning as intended by the ROD [Record of Decision on site cleanup]. Ground-water [sic] data from the monitoring well network at the*

> *site does not appropriately represent the concentrations of total toxaphene present in the ground water.*

The Corps believed the additional information provided by Region 4 supported this change in the protection determination. We initially did not agree. As discussed in this report, Region 4 should identify and measure both toxaphene and its breakdown products. However, since additional actions were taken to ensure that the community around the site is not exposed to the groundwater, we agree the remedy is effective.

Implement Recommendations Proposed by the Corps

Based on their review, the Corps recommended six corrective actions at the Hercules 009 Landfill. Although we agree with all of them, we were particularly interested in the three related to the groundwater. One of these three concerned testing for toxaphene breakdown products, which we addressed in Chapter 2 of this report. Another concerned the deed restrictions to control future land use. The third concerned verifying that no one in the vicinity is using the groundwater. The latter two recommendations should be implemented immediately because doing so would further protect human health while the testing issue is resolved.

As part of the cleanup, restrictions were to be placed in the property deed to limit using the land, and to prevent excavating at the site and using the groundwater. The Corps did not find such deed restrictions in the property records. Therefore, ~~the Corps recommended that, with EPA oversight, Hercules Incorporated place~~ deed restrictions to control future land use. According to the RPM, this recommendation is being addressed.

To address the threat of contaminated groundwater that could affect residential drinking wells down gradient of the Hercules 009 Landfill, in December 1992, the municipal water lines were extended to reach the residents adjacent to the site. Later, the private wells of the residents who received municipal water were to be properly abandoned. The document summarizing the cleanup actions taken at the site did not confirm that all private wells were properly abandoned. The Corps recommended that EPA make sure no one is still on private wells and that no one has put in new wells in that area.

Recommendation

3.1 We recommend that the Regional Administrator, Region 4, issue the report on the Hercules 009 Landfill 5-year review.

Agency Comments and OIG Evaluation

The draft report contained three recommendations in Chapter 3, all of which the Region 4 officials disagreed with. We removed the second and third of the three recommendations because Region 4 provided documentation that (1) the consent decree was recorded in the records of Glynn County, and (2) Hercules Incorporated investigated the status of wells in the immediate area of the Hercules 009 Landfill and concluded that no new private drinking water wells were installed. Thus, no one in the vicinity of the site was using the groundwater. A Region 4 hydrologist evaluated the perimeter monitoring well system and concluded it is sufficient to evaluate migration of contaminants. The hydrologist's report was Attachment 4 to the Region 4 response.

The remaining recommendation in the draft report was that the Regional Administrator, Region 4, issue the report on the Hercules 009 Landfill 5-year review with the conclusion that whether the groundwater cleanup protects human health cannot be determined at this time, and further evaluation is needed. A timeframe should be estimated for such an evaluation.

Because of the recent evidence (see Chapter 2) provided by the NIMS data and the toxicity criteria developed by Region 4 based on the MATT laboratory study, Region 4 proposed that the data and toxicity review be included in the release of the 5-year review and a determination of protectiveness be issued. They believed this position was further supported by their above conclusions that no one was using the groundwater and the contaminants (if any) were not leaving the site.

The OIG agrees with Region 4 that there appears to be no pathway for toxaphene breakdown products in the groundwater to reach people near the site. Therefore, we revised the recommendation to require the report on the 5-year review be ~~issued. The report can state that the remedy is effective and protects human~~ health, although our reasons, as discussed in more detail in Appendix C, differ slightly from those of Region 4.

Appendix A

Technical Discussion on Toxaphene

In order to evaluate the continued effectiveness of the Hercules 009 Landfill remedy, the Record of Decision (EPA/ROD/R04-93/144) requires periodic testing of the groundwater for toxaphene contamination. Both Hercules Incorporated and the U.S. Environmental Protection Agency (EPA) use EPA's analytical Method 8081 to test for the original toxaphene pesticide mixture in the groundwater. However, the original toxaphene pesticide mixture is known to degrade in the environment and its degradation products are probably at least as toxic as the original toxaphene pesticide. Since EPA's monitored natural attenuation guidance requires EPA to anticipate and to test for the presence of potentially toxic degradation products in the groundwater, EPA is required to evaluate the groundwater around the Hercules 009 Landfill Superfund site for the potential presence of toxaphene degradation products. However, analytical Method 8081 was not designed for and is inadequate to detect and measure toxaphene degradation products. Therefore, EPA needs to use a different analytical method, such as negative ion mass spectroscopy, to definitively assess the presence or absence of toxaphene degradation products in the groundwater at the Hercules 009 Landfill site.

Basics of Toxaphene Chemistry

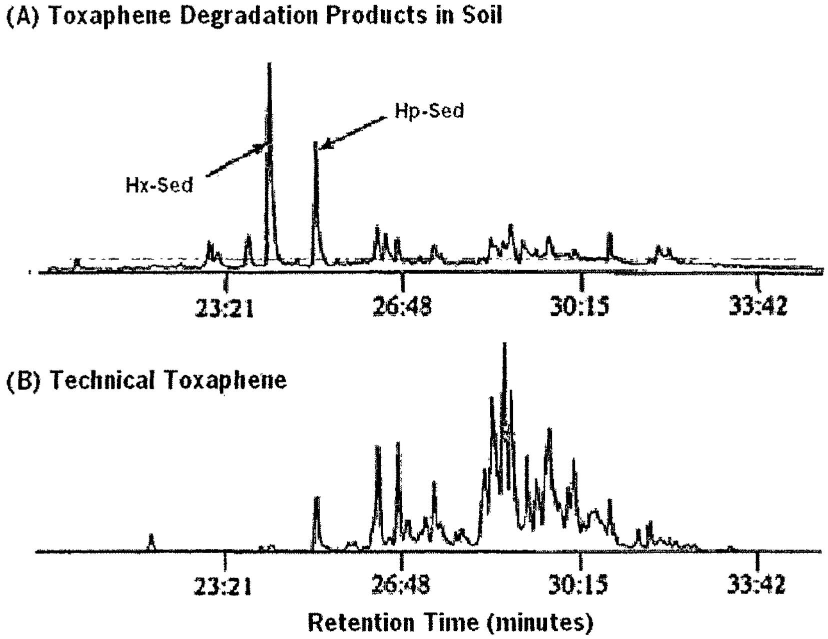
A basic understanding of the chemical structure of toxaphene is needed to address the issue. Unlike most organic environmental pollutants, toxaphene is not a single organic compound. As manufactured, the original toxaphene pesticide is a mixture of more than 200 closely related chlorinated organic compounds. This original toxaphene pesticide mixture is commonly known as "technical" toxaphene. Technical toxaphene consists mainly of polychlorinated bornanes with between six to nine chlorines attached. The term, congener, is used to refer to a single, structurely-unique constituent of the mixture. In other words, at least 200 individual toxaphene congeners make up the original toxaphene pesticide mixture. Individual congeners are often given their own names, such as Hx-Sed, Hp-Sed, p26, or p50.

Technical Toxaphene Degrades in the Environment

In the Office of Inspector General's (OIG's) review of the available scientific literature on the environmental degradation of the original toxaphene mixture (a.k.a. technical toxaphene), we found numerous references to biotic and abiotic degradation, and to aerobic and anaerobic degradation. The aerobic degradation of technical toxaphene occurs at the slowest rate and has an aerobic half-life report of about 10-14 years (Fingerling 1996). On the other hand, anaerobic degradation of technical toxaphene occurs at a much faster rate and has an anaerobic half-life of about 6 weeks. Therefore, since the use of toxaphene was severely restricted in 1982 (i.e., about 23 years ago), any technical toxaphene left in the environment from 1982 or before has theoretically undergone two or more half-lives. Thus, at most, only 25 percent of the original starting material should theoretically still be present. By contrast, the only reported condition under which toxaphene does not degrade is autoclaved soil (i.e., all microbes in the soil have been killed off) (Fingerling 1996). Therefore, technical toxaphene is expected to degrade in the environment and its degradation is mediated primarily by microbes living in the soil.

Anticipated Toxaphene Degradation Products

Upon instrumental analysis by a Gas Chromatograph/Electron Capture Detector (GC/ECD), the original technical mixture (i.e., a mixture of 200 or more congeners) produces a complex, multi-peaked chromatogram (see Figure 1B below). However, technical toxaphene is known to undergo microbial degradation in soil. Since the soil at the Hercules 009 Landfill site has been stabilized with cement, the free exchange of oxygen into the soil from the air is unlikely. Therefore, anaerobic microbial degradation is the most likely degradation process for the buried toxaphene waste at the Hercules 009 Landfill site.


(A) Toxaphene Degradation Products in Soil

(B) Technical Toxaphene

Figure 1: Chromatograms of Technical Toxaphene and Degraded Toxaphene are Completely Different

The major anaerobic microbial degradation products in soils or sediments are known to be Hx-Sed and Hp-Sed (Braekevelt 2001). This microbial degradation of technical toxaphene produces a much simplified chromatogram (see Figure 1A above). Therefore, upon analysis at an environmental laboratory, the degraded toxaphene chromatogram appears completely different then the technical toxaphene chromatogram.

Although Hx-Sed and Hp-Sed are the major anaerobic degradation products in soil, degraded toxaphene chromatogram (see Figure 1A) also shows a significant number of other, less abundant anaerobic microbial degradation products. These less abundant toxaphene congeners in soil have been identified and are known to include the p26, p50, p40, p41, and p44 (Maruya 2001). As discussed in more detail later, these less abundant toxaphene degradation products constitute the majority of risk to human health because they are not effectively metabolized by the body, which causes them to bioaccumulate in the body. Hx-Sed and Hp-Sed are readily metabolized by the body and excreted, so they should not constitute a major risk to human health. However, since Hx-Sed and Hp-Sed are the major anaerobic degradation products, they are easier to detect than the other less abundant toxaphene congeners and could be used to indicate that toxaphene degradation products are present in the sample.

The implication of toxaphene's degradation is that humans are exposed to toxaphene's degradation products and not to the original technical toxaphene mixture (de Geus 1999), (McHugh 2003). Consequently, EPA's approach of using Method 8081 to test for the original technical toxaphene in the environment to identify toxaphene contamination is incorrect. EPA needs to test for individual toxaphene degradation products (i.e., specific congeners) in order to identify the presence or absence of toxaphene contamination in the environment.

Evaluating the Potential Risk to Humans from Toxaphene Exposure

Conducting a detailed and comprehensive risk assessment for the potential exposure to toxaphene from the Hercules 009 Landfill site is a complex task that is beyond the scope of this OIG review. Detailed information is lacking on the potential human exposure to toxaphene degradation products and their toxicity, which limits the ability to conduct a thorough risk assessment. However, the potential risk to human health from toxaphene exposure can still be conceptually understood.

In general, a major factor needed to evaluate the level of risk to human health is to determine the major human exposure pathways to toxaphene's degradation products and to determine all potential sources. The Hercules 009 Landfill site is just one of the potential exposure sources. A toxaphene exposure study from the Netherlands used an EUSES (European Union System for the Evaluation of Substances) model to estimate the exposure of the Dutch population to toxaphene (Fiolet and van Veen 2001). This model identified that the main route of exposure to relatively soluble toxaphene congeners is approximately 80 percent from fish and 11 percent from drinking water. Another toxaphene exposure study by Buranatrevedh also concluded that the main route of exposure is about 93 percent from fish and about 7 percent from surface waters (Buranatrevedh 2004). Based on these national toxaphene exposure studies, the main exposure risk to toxaphene is clearly from fish (i.e., 80-93 percent) and from potential sources of drinking water (i.e., 7-11 percent). Although specific site conditions and other site specific variables at Hercules 009 Landfill will shift the relative levels for these various exposure routes, these national toxaphene exposure studies identify that the principle exposure routes of concern to the surrounding community are the fish in the diet and the potential for contaminated drinking water. The remaining exposure routes (i.e., air and soil) are practically negligible.

Another major factor needed to evaluate the level of risk to human health is what specific toxaphene congeners pose chronic risk to humans. The major toxaphene congeners found in fish are p26, p50, and p62, but p40, p41, and p44 are also present to a lesser extent (Fiolet and van Veen 2001). The major anaerobic microbial degradation products in soils that may contaminate the groundwater are Hx-Sed and Hp-Sed, but p26, p50, p40, p41, and p44 are also found in soil to a lesser extent (Maruya 2001).

Although humans are exposed to a variety of toxaphene degradation congeners, most of these congeners can be rapidly metabolized via dechlorination, dehydrodechlorination, and oxidation, primarily through the action of the mixed function oxidase system and other hepatic microsomal enzymes (EPA 1999). For example, the primary toxaphene degradation products in soil (i.e., Hx-Sed and Hp-Sed) are expected to be easily metabolized and excreted with reported half-lives in fish of 5 and 13 days respectively (Smalling 2004). However, a limited number of toxaphene congeners (i.e., p26, p50, p40, p41) are poorly metabolized and cannot be readily excreted, causing these congeners to accumulate in the body. These poorly metabolized congeners share a common structural pattern of alternating single chlorine substitutions (i.e., endo, exo) on the #2, #3, #5, and #6 carbons of the six-member ring (Maruya 2000). Specifically, the poorly metabolized p26 and p50 congeners have half-lives of about 1 year in wild fish (Smalling 2004). Therefore, although humans are exposed to a variety of toxaphene degradation products, the human body can metabolize and eliminate the majority of these congeners. However, five toxaphene congeners (i.e., p26, p50, p 40, p41, and p44) are not readily metabolized and excreted ~~and, thus, can accumulate in the human body~~.

To evaluate the level of risk to human health, EPA needs to know the concentration of these five congeners and their metabolite precursors in the environment. Since these five toxaphene congeners represent the long-term chronic toxaphene exposure problem to humans, the toxicity of these five individual congeners and/or a mixture of these five congeners needs to be determined in more detail than is currently available in the scientific literature.

Human Exposure to the p26 and p50 Toxaphene Degradation Congeners

The following two academic studies have independently identified and documented human exposure to the individual toxaphene degradation congeners:

- In 1996, Dr. Gill used negative ion mass spectroscopy (NIMS) to detect and measure toxaphene congeners in human blood serum (Gill, et al. 1997). Specifically, Dr. Gill's study documented the presence of p26, p50, p44, p40, and p41 congeners at a concentration of 2 to 200 parts per trillion (ppt) or up to 0.2 parts per billion (ppb) in human blood serum from Native Canadian Communities. These five toxaphene congeners represented 95 percent of the toxaphene congeners found in human serum.

- In 2003, Dr. Barr used a sophisticated analytical technique to detect and measure toxaphene congeners in pooled human blood serum collected by the Red Cross in Atlanta in 1987, in Chicago in 1992, and in Cincinnati in 1994 (Barr 2004). Specifically, Dr. Barr's study documented the presence of p26, p50, and possibly p40+41, and p44 congeners at a concentration of 3 to 30 ppt (i.e., 0.03 ppb) in human blood serum from an undefined number of American blood donors.

These studies are critically important in identifying and simplifying the assessment of the risk to humans resulting from environmental exposure to toxaphene. These studies dramatically indicate that human risk is not to "technical" toxaphene's 200-plus congeners, but that the long-term chronic toxaphene exposure in humans is limited and simplified to just five toxaphene congeners (i.e., p26, p50, p40, p41, and p44) that the human body has difficulty metabolizing and eliminating, causing them to accumulate in the body.

Carcinogenicity of p26 and p50 Congeners

The EPA's Integrated Risk Information System (IRIS) database identifies technical toxaphene as a B2 probable human carcinogen with a cancer potency factor of 1.1 mg/kg/day. However, there is limited scientific data on the carcinogenicity of persistent toxaphene degradation congeners, such as p26 and p50. But other chemical mixtures of congeners show that individual congeners can be significantly more carcinogenic then the original technical mixture. The classic example is dioxin where 2,3,7,8-TCDD (tetrachlorodibenzo-p-dioxin) is up to 10,000 times more carcinogenic than other dioxin congeners. Another example is that bioaccumulated PCB congeners appear to be more carcinogenic than the original "commercial" PCB mixture (EPA 7C-R293-NTSX). This clearly indicates that the carcinogenicity of the original technical ~~toxaphene mixture cannot be applied to the carcinogenicity~~ of ~~the individual congeners,~~ specifically, p26 and p50.

The European Union has conducted an Investigation into the Monitoring, Analysis, and Toxicity of Toxaphene in Marine Foodstuffs (i.e., MATT project). The MATT project predicted the tumor-promoting potency of technical toxaphene and a Cod Liver Extract (CLE) containing p26, p50, p62 in a bioassay measuring the inhibition of intracellular communication between Hepa1c1c7 cells (Fair CT PL.96.3131). The CLE toxaphene congener mixture mimics the environmental exposure to the toxaphene congeners that are found in humans (e.g., p26 and p50). The results from this bioassay indicate that the CLE toxaphene mixture is a more potent tumor promoter than the original technical toxaphene mixture. The MATT project estimated a tolerable daily intake (TDI) to "weathered" toxaphene residues of 0.69 mg/kg/day. In general terms, MATT's TDI estimate makes the toxaphene degradation products found in humans to be about twice as carcinogenic as the original technical toxaphene mixture. However, more definitive toxicology studies are needed to verify the carcinogenicity of the individual p26 and p50 toxaphene congeners.

Embryotoxicity of p26 and p50

In a 1997 study using a rat embryo culture model, the p26 and p50 toxaphene congeners caused abnormalities in the central nervous system (Calciu 1997). The total morphological scores at 100 ng/ml for p26 and p50 were slightly worse than the total morphological score for the technical toxaphene. The significant finding from this study is that both the target site and type of toxicity are highly congener-specific. Therefore, the toxicity of technical toxaphene cannot and should not be used to predict the embryotoxic effects of the p26 and p50 congeners in humans. Thus, more scientific research is needed to evaluate the specific embryotoxic effects of p26 and p50 to humans.

Dr. Gill's study found concentrations of p26 and p50 at concentrations as high as 0.2 ppb in human blood serum (described above). The lowest dose in Dr. Calciu's rat embryo culture study was 100 ppb. The difference is a factor of 500, but the rat embryo culture study results represent only a 48-hour exposure to the rat embryos. This short exposure time does not directly correspond to human exposures to p26 and p50 over the full term of a pregnancy (i.e., human fetuses are exposed to a lower dose but for a longer period of time). Furthermore, the results from the rat embryo culture study represent dramatic development changes in which even subtle changes in human fetal development would be considered unacceptable. Therefore, additional research is needed to evaluate the potential for more subtle effects on embryo development when exposed to lower doses of p26 and p50 that correspond to actual human exposure levels. For example, in 1980, Dr. Olson observed behavior changes in rat offspring when pregnant rats were given low doses of technical toxaphene, p42a congener (i.e., toxicant A), or p32 congener (i.e., toxicant B) as measured by swimming test and maze retention test (Olson 1980).

The embryotoxicity of toxaphene's persistent degradation products needs to be evaluated in the context of co-exposure with other persistent organochlorines (i.e., dichlorodiphenyltrichloroethane (DDT)/dichlorodiphenuldichloroethylene (DDE), hexachlorocyclohexanes (HCHs), and polychlorinated biphenyls (PCBs)). The amount of p26 and p50 in human milk has been found to range from a low of 6 ug/kg lipid weight (i.e., ppb) in ~~southern Canada to a high of 294 ug/kg lipid weight in Northern Quebec (Skopp, S., et al. 2002).~~ This shows that babies are exposed through the mother's exposure to toxaphene degradation products before and after birth. Unfortunately, this observation about mother's milk is potentially problematic because an epidemiological study by Jacobson (Jacobson 1996) indicates that developing embryos are the most susceptible target of organochlorines (i.e., PCBs). Jacobson's study linked organochlorine exposure during fetal development to impaired cognitive development (e.g., low IQ scores). Therefore, the embryotoxicity from toxaphene exposure needs to be evaluated in combination with the concurrent exposure to the other organochlorines (i.e., DDT/DDE, HCHs, and PCBs) in order to accurately assess the risk to cognitive impairment.

Superfund's Remedy Requires the Evaluation of Toxic Degradation Products

Monitored natural attenuation (MNA) is part of the remedy at Hercules 009 Landfill site. Superfund's monitored natural attenuation guidance (OSWER Directive 9200.4-17P) requires EPA to evaluate for the potential presence of toxic transformation products. Toxaphene degradation products are a sub-category of transformation products. Specifically, the MNA guidance states:

> "*The potential for creation of toxic transformation products is more likely to occur at non-petroleum release sites ... and should be evaluated to determine if implementation of a MNA remedy is appropriate and protective in the long term.*"

Furthermore, the MNA guidance states:

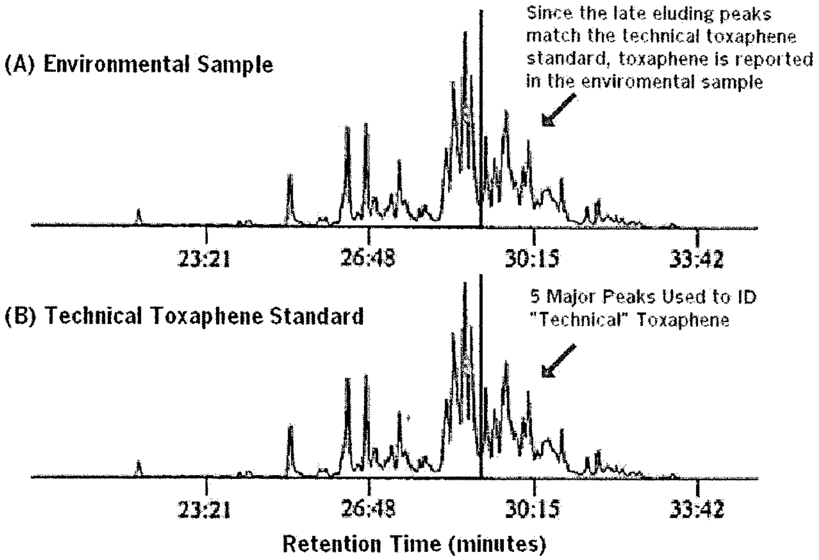
> "*... all [MNA] monitoring programs should be designed to accomplish the following: ... Identify any potentially toxic and/or mobile transformation products.*"

Therefore, the Superfund's MNA guidance requires EPA to anticipate and to test for the presence of potentially toxic degradation products at hazardous waste sites. Since toxaphene is known to degrade in the environment and these degradation products are thought to be toxic, EPA must evalaute the groundwater at the Hercules 009 Landfill site for toxaphene's degradation products, specifically, the Hx-Sed and Hp-Sed congeners, but also the p26, p50, p40, p41, and p44 congeners.

EPA Method 8081 Tests for Technical Toxaphene

EPA Method 8081 is an analytical testing technique that uses a laboratory instrument called a gas chromatograph with an electron capture detector, which is referred to as a GC/ECD. When an environmental sample is tested by the GC/ECD, the instrument products a chromatogram as a record of what was contained in the sample (see Figure 2A).

Each peak in the chromatogram of a known technical toxaphene standard (see Figure 2B) represents 1 of the 200 unique congeners in the technical toxaphene mixture. There are actually so many peaks that they clump together in some areas of the chromatogram. Method 8081 detects toxaphene by identifying five peaks to the right of the red line in the environmental sample (see Figure 2A) and comparing their shape and position to five peaks to the right of the red line in a known technical toxaphene standard (see Figure 2B). In this example, since both chromatograms match on the right hand side, the laboratory would report that toxaphene is present in this hypothetical enviromental sample. EPA Method 8081 was designed and quite dependable for detecting the original technical toxaphene mixture in an environmental sample.


(A) Environmental Sample

Since the late eluding peaks match the technical toxaphene standard, toxaphene is reported in the enviromental sample

(B) Technical Toxaphene Standard

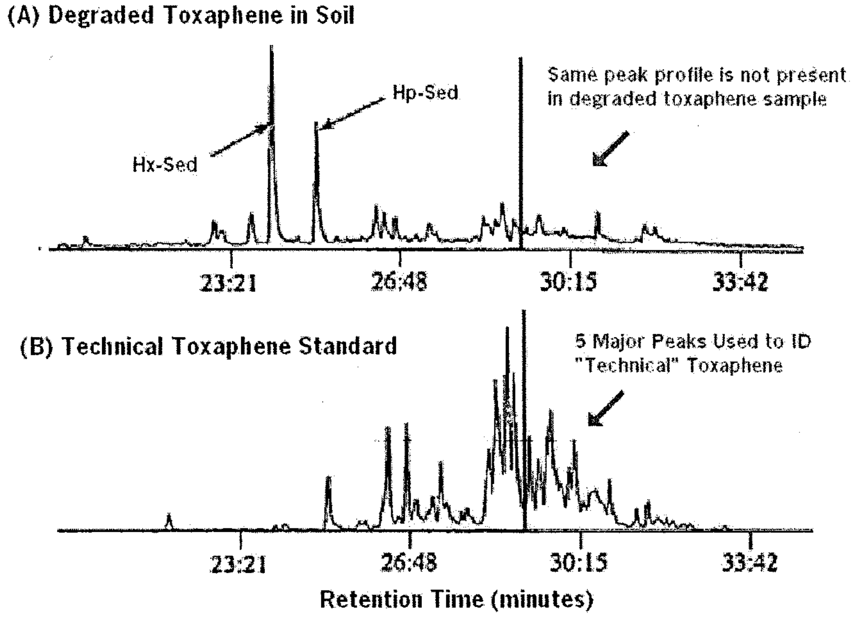
5 Major Peaks Used to ID "Technical" Toxaphene

Figure 2: GC/ECD Chromatograms of Technical Toxaphene

EPA Method 8081 Does Not Identify Toxaphene Degradation Products

EPA Method 8081, which is listed in EPA's Test Methods for Evaluating Solid Waste, Physical/Chemical Methods (i.e, SW-846), uses a GC/ECD to analyze for the presence of toxaphene contamination. In order to identify the presence of a pollutant in an environmental sample, the retention time of a peak (i.e., representing a compound) in the sample's chromatogram is compared against the retention time of a known chemical standard. However, technical toxaphene is not a single compound, but a mixture of more than 200 chlorinated bornanes which produces a complex chromatogram (see Figure 3B below). For the purposes of detecting toxaphene in a sample, EPA Method 8081 calls for a peak profile match against at least five peaks in the latter section of the toxaphene window (i.e., see the peaks after about 29 minutes in the chromatogram 3B). In other words, the observed relative abundance of late eluting toxaphene congeners (i.e., octa- and nonachlorobornanes) has to closely match the relative abundance of the octa- and nonachlorobornane congeners found in the technical toxaphene standard. EPA Method 8081 is appropriate and highly accurate for detecting technical toxaphene. However, EPA Method 8081 is not effective for detecting degraded toxaphene (i.e., "weathered" toxaphene) in environmental samples (e.g., soil, water, fish).

For demonstration purposes, chromatogram 3A below is a known chromatogram of toxaphene degradation products in soils. When chromatogram 3A is compared by EPA Method 8081's identification criteria for technical toxaphene, chromatogram 3A obviously does not have the same late eluding peak profile (i.e., the peaks after 29 minutes) as the technical toxaphene standard. Therefore, a match is not made and the presence of toxaphene is not reported by the laboratory, even though specific toxaphene congeners (e.g., Hx-Sed and Hp-Sed) are known to be present. This example demonstrates the manner in which EPA Method 8081 fails to detect toxaphene degradation products (i.e.,"weathered" toxaphene or individual toxaphene congeners) in environmental samples.



(A) Degraded Toxaphene in Soil

(B) Technical Toxaphene Standard

Figure 3: EPA Method 8081 Analyzes for Only Technical Toxaphene

An example of EPA Method 8081's failure to detect toxaphene's degradation products occurred in 1997 during the Georgia Department of Natural Resources' (GA/DNR) study to measure the toxaphene levels in several species of fish and shellfish in and around Terry Creek. Terry Creek is another Superfund site in the Brunswick, Georgia, area that is contaminated with toxaphene due to previous manufacturing operations by Hercules Incorporated. The results of GA/DNR's study indicated no detectable quantities of toxaphene in every single fish sample analyzed. However, in 2001, Dr. Maruya re-analyzed the same fish and shellfish samples that were collected and analyzed by GA/DNR, but this time used a congener-specific technique called Gas Chromatography/Negative Ion Mass Spectroscopy (GC/NIMS) (Maruya 2001). The GC/NIMS analytical technique was able to identify and quantify individual toxaphene congeners that were present in the fish samples at concentrations up to 1,420 parts per billion (ppb). The GC/NIMS's identification of toxaphene contamination at Terry Creek is in stark contrast to the results obtained by EPA Method 8081 that indicated no toxaphene contamination. Therefore, this example clearly shows that EPA's Method 8081 does not detect degraded toxaphene in the environment.

Gas Chromatogaph/Negative Ion Mass Spectrometry Can Be Used to Identify Toxaphene Degradation Products

Unlike the GC/ECD technique used in EPA Method 8081, GC/NIMS can definitively identify and measure individual toxaphene degradation products in the environment. The weakness in the GC/ECD technique used in EPA Method 8081 is that peak identification is based on only one factor: retention time. Therefore, even if the retention times match between the sample peak and the standard, there is still uncertainty about the identity of the peak. By contrast, the GC/NIMS technique uses two factors to identify peaks: retention time and a mass spectrum. A mass spectrum is analogous to a "fingerprint" of the compound. If the mass spectrum from the sample matches the mass spectrum of the standard, this definitively identifies the compound.

The GC/NIMS methodology has been routinely used in academia since about 1993. The European MATT project has been using the GC/NIMS method to monitor and document the levels of toxaphene degradation products in fish from the North Atlantic. Since the GC/NIMS method has been developed and successfully implemented by others, EPA's formal validation and standardization of the GC/NIMS method should not present any major technical difficulties. Also, including the GC/NIMS method in SW-846 would significantly facilitate (1) evaluating toxaphene degradation products in the environment by the regulated community and (2) ~~gathering congener-specific data needed for accurate risk assessments of exposure to~~ toxaphene's degradation products.

Estimated Retention Time of Toxaphene Degradration Products

As described, EPA Method 8081 fails to identify toxaphene degradation products mainly because the identification criteria are based on seeing the late eluting peaks in technical toxaphene. However, an experienced chemist can still look for potential toxaphene degradation products in the GC/ECD data from the Hercules 009 Landfill. Although the Hercules 009 GC/ECD data does not include standards for the Hx-Sed and Hp-Sed toxaphene degradates, the expected retention time for Hx-Sed and Hp-Sed can be estimated from data published in the scientific literature (Figure 4 below). Since each technical toxaphene varies slightly by manufacturer, the technical toxaphene standard below is specifically from Hercules Incorporated in order to allow a subsequent comparison with the Hercules 009 Superfund site data. The estimated retention time window for the Hx-Sed and Hp-Sed toxaphene congeners (i.e., the main toxaphene congeners expected in anaerobic soil) occurs at the front edge of the technical toxaphene window. Notice that the Hx-Sed peak is to the left and taller than the Hp-Sed peak.

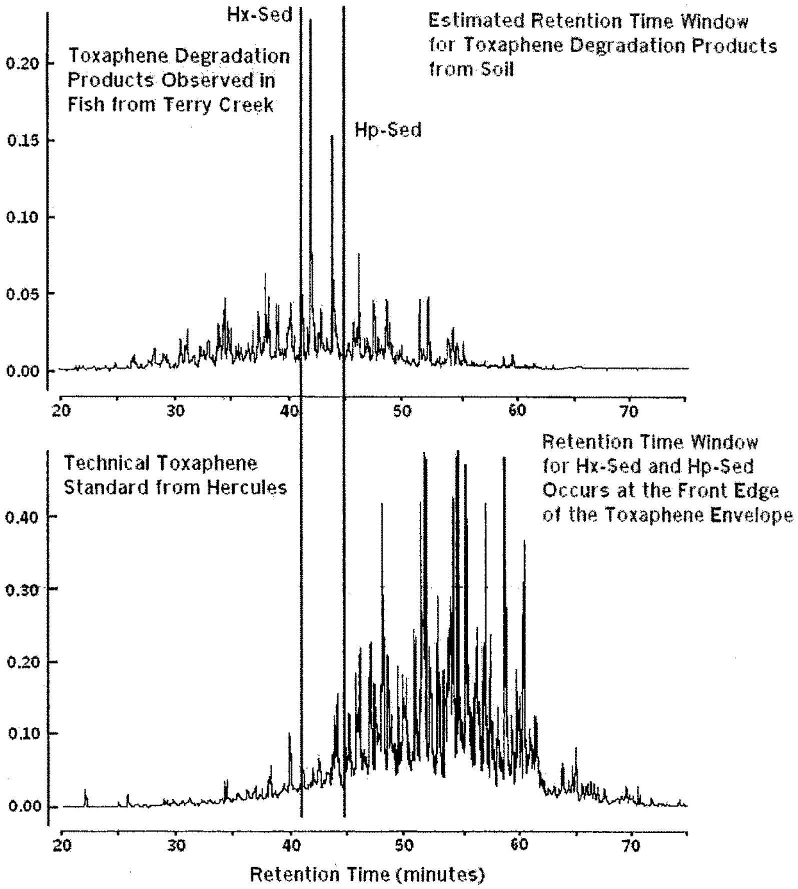
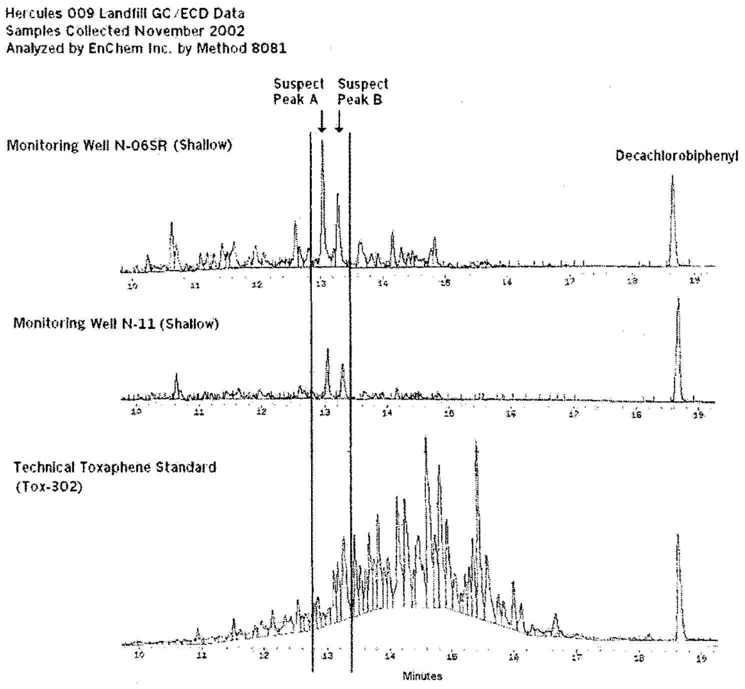


Figure 4: Estimated Retention Time Window for Hx-sed and Hp-sed

Hercules 009 GC/ECD Data Suggest Toxaphene Degradation Products May Be in the Groundwater

On January 8, 2003, the contractor for Hercules Incorporated, RMT Incorporated, provided EPA with the November 2002 groundwater sampling results, which were used in EPA's Hercules 009 Landfill 5-year review. RMT's subcontract laboratory (i.e., EnChem, Inc.) used EPA Method

8081A to analyze the toxaphene groundwater samples and reported non-detect (i.e., <5.2 ug/L) for all toxaphene results. Fortunately, the sampling results included a chromatogram for each of the groundwater monitoring wells. This allowed for comparing the Hercules 009 Landfill groundwater samples against the Hercules technical toxaphene standard to check for the possibility of toxaphene degradation products (Figure 5 below).



Note: Chromatograms are normalized to the surrogate compound (Decachlorobiphenyl)

Figure 5: Potential Toxaphene Degradation Products in the Groundwater at Hercules 009 Landfill

As described above in the previous section, the estimated retention time window for the Hx-Sed and Hp-Sed toxaphene congeners occurs at the front edge of the technical toxaphene window. When the estimated retention time windows for Hx-Sed and Hp-Sed are superimposed on the chromatograms from monitoring wells N-06SR and N-11, two prominent peaks are present that resemble the Hx-Sed and Hp-Sed peak profile (i.e., the left peak is taller than the right peak). These chromatograms provide suggestive evidence that Hx-Sed and Hp-Sed might be present in the Hercules 009 Landfill groundwater. However, these peaks cannot be positively identified as toxaphene degradation products due to significant limitations in the data set. First, there are no Hx-Sed or Hp-Sed standards to establish their retention time, which is the key criterion for identifying compounds in a GC/ECD analysis (i.e., no standards, no identifications). Second, the critical weakness with all GC/ECD data is the lack of a mass spectrum that could be used to determine the structure of the compound making each of these peaks. The limitations of this GC/ECD data set clearly show the value of GC/NIMS analysis.

If the samples had been run by GC/NIMS instead of GC/ECD, a quick review of the mass spectra for each of the peaks could easily determine if these peaks were toxaphene congeners or not (e.g., examples of negative ion mass spectra are provided in Figure 6). For example, the negative ion mass spectrum for Suspect Peak A could be compared against the negative ion mass spectrum of a hexachlorinated bornanes (Figure 6(a)). Likewise, the negative ion mass spectrum for Suspect Peak B could be compared against the negative ion mass spectrum of a heptachlorinated bornanes (Figure 6(b)). If the spectra matched, EPA could conclude that there were toxaphene degradation products in the groundwater. However, with only the GC/ECD data, a definitive determination on the identity of these suspect peaks cannot be made.

GC/NIMS Can Definitively Determine the Identity of Suspected Hx-Sed and Hp-Sed Peaks

GC/NIMS could be used to definitively determine the identity of the Suspect A and B peaks observed in the Hercules 009 Landfill GC/ECD data (see Figure 5). The retention time and mass spectrum for Suspect Peak A would be compared against the retention time and mass spectrum for Hx-Sed. The mass spectrum for Hx-Sed looks like the diagram in Figure 6(a). The retention time and mass spectrum for Suspect Peak B would be compared against the retention time and mass spectrum for Hp-Sed. The mass spectrum for Hp-Sed looks like the diagram in Figure 6(b). ~~The additional feature of the GC/NIMS technique of comparing and matching a peak's~~ mass spectrum allows for the definitive identification of the peaks.

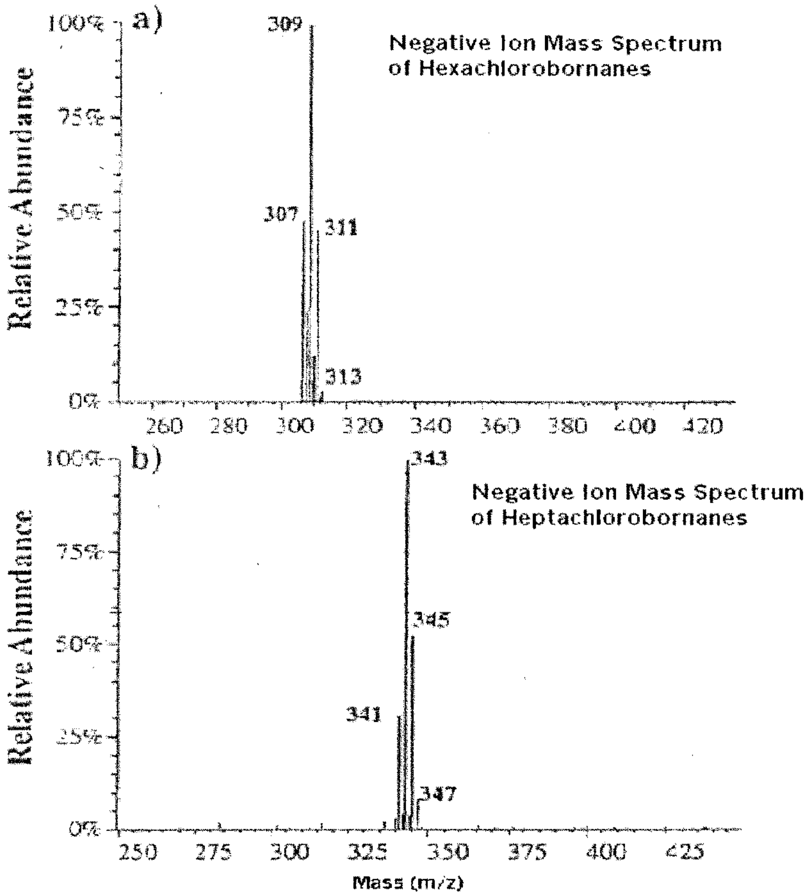


Figure 6: Negative Ion Mass Spectrums
for Hexachlorobornane and Heptachlorobornane

Technical Summary of Toxaphene Issue

EPA should recognize that toxaphene degrades in the environment and that all of EPA's toxaphene data collected using EPA Method 8081 are inadequate to screen for toxaphene's degradation products in the environment. To address this problem, EPA should test toxaphene contamination using a congener-specific analytical method such as GC/NIMS. EPA's validation and standardization of the GC/NIMS method would facilitate evaluating toxaphene degradation products in the environment. Finally, EPA should recognize that the chronic health risk to humans is from the five persistent toxaphene congeners (i.e., p26, p50, p40, p41, and p44) that accumulate in the human body. Therefore, EPA needs additional studies on the carcinogenicity and embryotoxicity of these five persistent toxaphene congeners to be able to accurately evaluate this risk associated with their exposure to humans. Without congener-specific laboratory results and without knowing the toxicity of specific congeners, EPA is unable to definitively quantify the risk to human health posed by the toxaphene degradation products left in the environment and the food chain.

No Immediate Human Health Risk at Hercules 009 Landfill

Although the OIG's review indicates that the current monitoring and analytical testing at the Hercules 009 Landfill site is inadequate to determine if any toxaphene degradation products have leaked into the groundwater and that these toxaphene degradation products may be toxic, the OIG believes that there is no immediate risk to the surrounding population because the remedial ~~action for Operable Unit Two has connected the nearby residents to the municipal drinking water~~ supply. However, to prevent the potential long-term contamination of the groundwater, EPA needs to definitively determine if Hx-Sed, Hp-Sed, p26, and/or p50 toxaphene congeners occur in the groundwater down gradient of the Hercules 009 site.

OIG Technical Conclusions

- The original "technical" toxaphene mixture degrades in the environment.
- The chronic health risk to humans is from exposure to toxaphene's persistent degradation products (e.g., p26, p50, p40, p41, and p44) and not the original technical toxaphene mixture.
- EPA needs to use a congener-specific analytical method (e.g., GC/NIMS) to positively identify and quantify toxaphene degradation products in the environment. The OIG highly recommends standardizing and validating the GC/NIMS method and inserting an EPA GC/NIMS method into SW-846.
- EPA needs to conduct specific research into both the carcinogenicity and embryotoxicity of the five persistent human toxaphene congeners (i.e., p26, p50, p40, p41, and p44) to develop acceptable human exposure limits to the individual congeners and/or to the mixture of these five congeners.

- Considering both the uncertainty as to whether the Hercules 009 Landfill sites groundwater is contaminated with toxaphene degradation products and the uncertainty about the human toxicity of these toxaphene degradation products, Superfund's 5-year review for the Hercules 009 Landfill site should conclude that whether the MNA remedy protects human health cannot be determined at this time. As a result of this uncertainty in the data, the Region needs to definitively determine if the groundwater is contaminated with the Hx-Sed and Hp-Sed toxaphene congeners generated by the microbial degradation of "technical" toxaphene.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION 4
ATLANTA FEDERAL CENTER
61 FORSYTH STREET
ATLANTA, GEORGIA 30303-8960

June 29, 2005

MEMORANDUM

SUBJECT: Comments on the Draft Ombudsman Report
Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site, Brunswick, Georgia; Assignment 2004-124

FROM: J. I. Palmer, Jr.
Regional Administrator

TO: Paul D. McKechnie
Acting Ombudsman
Office of Congressional and Public Liaison

Thank you for the opportunity to provide comments on the draft report. The following comments relate to the subject document, and are provided primarily to address the action required in EPA Manual 2750. In accordance with the memorandum transmitting the draft report, we have followed the instructions to "address the factual accuracy of the draft report and ~~indicate concurrence or noncurrence with each finding and proposed recommendation. If you do~~ not concur with the proposed recommendation, please provide any alternative actions you wish to be considered for the final report." The comments are a consolidation of input from Region 4's Analytical Support Branch of the Science and Ecosystem Support Division, and the Superfund Remedial and Technical Support Branch of the Waste Management Division. In addition, the Region has included comments from the Region 4 Office of Environmental Accountability (OEA) that address noted excerpts in the draft report.

Excerpt from the Draft Ombudsman Report Page 8, Recommendation 2.1:

"Use negative ion mass spectroscopy to definitely determine if toxaphene breakdown products are present in the surrounding groundwater at the Hercules 009 Landfill site, and (if so) in what amounts."

Response to Recommendation 2.1

The Region has used negative ion mass spectrometry (NIMS) to determine the presence of weathered toxaphene (WT). After the issuance of the Preliminary Technical Draft from the OIG, samples were collected from the 009 Landfill monitoring wells by Hercules, Inc., under a voluntary interim action on March 5th and analyzed by Keith Maruya at the Skidaway Institute of

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Oceanography using the NIMS method from a peer reviewed scientific publication. The Hercules, Inc., March 2005 Data Report is attached as an addendum.

Region 4's laboratory is willing to participate in a multi-laboratory method validation study for toxaphene congeners in environmental samples. However, since the Agency as a whole would obviously benefit from a validated NIMS method for toxaphene congeners, we believe that a multi-laboratory method validation study should be initiated at the program level by the Office of Solid Waste and Emergency Response. A validated method will serve both the regulated community and the Agency by assuring that analytical data produced by the method are defensible, of known quality, and suitable for risk assessment decision making.

Excerpt from the Draft Ombudsman Report, Page 8 Recommendation 2.2:

"If toxaphene breakdown products are found in the groundwater, assess the resulting risk to human health and take appropriate action."

Response to Recommendation 2.2

In response to the Preliminary Technical Draft from the OIG, Region 4 conducted a thorough literature review for information on the toxicity of WT and reached the following conclusions:

Application of the MCL to Groundwater at 009 Landfill
~~The NIMS analytical results from groundwater at the 009 Landfill are all significantly~~ less than the MCL for technical toxpahene (TT) of 3 ug/L. Based on the Region 4 preliminary toxicity assessment, it is reasonable to assume that this MCL is protective for WT as well as TT. The Region 4 Draft Report on WT toxicity is attached as an addendum and a short summary is provided below.

Toxicity Criterion for Weathered Toxaphene
To develop a human toxicity criterion for WT, three choices must be made: (1) the critical toxic endpoint; (2) the threshold dose value based on the critical endpoint; and (3) the uncertainty/safety factors applied to determine a reference dose.

Region 4 toxicologists believe that the most appropriate endpoint for WT is tumor promotion. This endpoint was chosen because it appears most relevant to humans, and focusing on this endpoint is also protective of other toxic endpoints, such as immunologic and developmental effects.

The Monitoring, Analysis and Toxicity of Toxaphene in Marine Foodstuffs (MATT) study from the European Union is the sole toxicological study based on WT and thus chemically is most relevant to human exposure. The critical study was performed in rats with changes in liver cells that represent precancerous changes as the endpoint. The no observable adverse effect level (NOAEL) from this study was 0.69 mg/kg-day as calculated by MATT or 0.6 mg/kg-day in the Region 4 analysis. Note these values are very similar.

The following uncertainty factors were considered: 10 for animal-to-human extrapolation and 10 for human variability. In spite of the paucity of studies on WT, the literature is replete with studies on TT that cover a range of endpoints. Many of these studies resulted in higher and less protective NOAELs. The studies that had similar values for NOAELs were ingestion or oral gavage studies based on TT. The bulk of toxaphene administered orally is excreted or metabolized quickly; hence, the internal doses of WT and TT and the subsequent toxaphene body burdens end up being of similar magnitude. Because of the large database of toxicity studies of TT, we believe no additional database insufficiency uncertainty factor was needed. Hence, the combined uncertainty factor is 100.

This derivation of a reference dose for WT based on tumor promotion is consistent with the recently finalized EPA cancer guidelines which state that the consideration of mode of action vis-à-vis toxicity is paramount in the development of a toxicity criterion.

The Need for Peer Review

Unfortunately, the laboratory studies on WT toxicity that the MATT report relied on have not yet undergone peer review because of logistical issues (one of the authors moving to a new university). Region 4 agrees with the OIG report that additional toxicity studies may be helpful. Peer review would also be helpful in elucidating some of the apparent errors in interpretation of EPA cancer potency factor derivation identified in the MATT report.

On page 19 of the OIG report, the MATT was quoted as indicating that WT is approximately twice as carcinogenic as TT. This statement of the MATT report is incorrect and unfortunately repeated in the OIG report. It is not entirely clear on what basis the MATT report makes this statement, but there are two possibilities.

First, the MATT report presented a misunderstanding of the EPA TT slope factor in which the MATT confused the units. The upshot of this misunderstanding is that the MATT toxicity criterion appears for WT about twice as stringent at the EPA toxicity criterion for the original TT mixture. In truth, the EPA toxicity criterion is 300 times more stringent than the MATT criterion.

Second, the MATT interpreted some empirical data obtained from a cell culture system and possibly made a large and unfounded conceptual leap. In this cell culture system, the toxic endpoint was disruption of intercellular communication. Calculations indicated that the WT was twice as effective in blocking intercellular communication as TT. However, to make the leap of claiming that effects on intercellular communication in a cell culture system is tantamount to a carcinogenic response in a whole animal is a very large leap indeed. This conceptual leap is not endorsed by Region 4 toxicologists.

Interim Strategy for Risk Assessment
In keeping with the OIG intention of using the best available science, Region 4 has two proposals for an interim strategy. The preferred approach is to use the toxicity criterion for WT developed by Region 4 Technical Services and based on the laboratory study in the MATT. Presently, the Region 4 report is still in draft, but should be finalized relatively soon. Hence, Region 4 requests that the OIG review both the MATT laboratory study and the Region 4 derivation of toxicity criteria to determine their soundness and applicability. An alternative approach is to use a toxicity criterion based on TT. The EPA toxicity criterion for TT now on IRIS was last revised in 1991. The toxicity value is based on rodent bioassays conducted in 1978 and 1979. In 2000, Goodman[1] reanalyzed these data using newer methods based on EPA guidance and concluded that TT was actually tenfold less toxic than the IRIS value. Region 4 believes that our preferred approach represents the best available science and would provide a reasonable interim approach.

Excerpt from the Draft Ombudsman Report Page 13, 3.1:

"Issue the report on the Hercules 009 Landfill 5-year review with the conclusion that the protectiveness of the groundwater cleanup cannot be determined at this time, and further evaluation is needed. A timeframe should be estimated for such an evaluation."

Response to Recommendation 3.1:

Based on the recent evidence provided by the NIMS data and the toxicity criterion developed by Region 4 based on the MATT laboratory study, Region 4 proposes that the data and toxicity review be included in the release of the 5-year review and a determination of protectiveness be issued.

Excerpt from the Draft Ombudsman Report Page 13, 3.2 :

"Ensure that restrictions are placed in the property deed to control future use of the land and groundwater."

Response to Recommendation 3.2:

When Hercules, Inc., entered into the Consent Decree for RD/RA with the U.S., it agreed to perform all operation and maintenance activities required to maintain the effectiveness of the

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[1] Goodman JI, Brusick DJ, Busey WM, Cohen SM, Lamb JC, Starr TB. (2000) Reevaluation of the cancer potency factor of toxaphene: recommendations from a peer review panel. Toxicol Sci. 2000 May;55(1):3-16.

Remedial Action. As set out in the Record of Decision, operation and maintenance of the multi-media cover was to continue for a minimum of 30 years. (See Section 9.A.1). The Consent Decree for RD/RA requires Hercules, Inc., to not only record a certified copy of the Consent Decree with the Glynn County registry of deeds, but to also include within any instrument conveying any interest in the property a notice describing the restrictions applicable to the property, the provisions of the Consent Decree with respect to institutional controls and EPA's right of access, and the obligations of successors-in-title. In addition, Hercules, Inc., and any successor-in-title must provide written notice to EPA of any proposed conveyance of any interest in the title. As part of EPA's statutory mandate for a 5-year review of a remedy's effectiveness if waste is left in place, the Consent Decree for RD/RA further obligates Hercules, Inc., to conduct any studies and investigations that EPA might request in support of its 5-year review. Moreover, no conveyance by Hercules, Inc., of any interest in property, however minor, will release or otherwise affect the liability of Hercules, Inc., to comply with the terms of the Consent Decree for RD/RA.

In light of the fact that the remedy has achieved the performance standards established in the Record of Decision and is believed to be currently performing as designed, EPA's statutory authorities and the enforcement-based tools arising from the Consent Decree for RD/RA are presently believed to be adequate institutional controls. Of course, if environmental or other conditions change, existing State-based legal authorities may in the future also be utilized to facilitate proprietary controls, such as an environmental easement designed to protect groundwater, if determined by EPA to be necessary.

Excerpt from the Draft Ombudsman Report Page 13, 3.3:

"Confirm that no one in the vicinity is using the groundwater."

Response to Recommendation 3.3 :

Since the perimeter monitoring wells are properly functioning as an intended early warning system, it becomes unnecessary to document private well water use outside the perimeter. Nonetheless, Hercules, Inc. has investigated the status of private registration of new wells in the immediate area. In checking with the Glynn County Environmental Department, Hercules was informed that the County has no record for the past several years of anyone advising them of the intent to drill a private drinking water well in the immediate area of the 009 Landfill. Hercules has also been informed by the previously affected residents that they continue to use city water for drinking purposes. Finally, Hercules has conducted a visual canvassing of the area to locate well house structures. This effort indicates that no new private drinking water wells have been installed in the immediate area surrounding the site.

The perimeter well monitoring system has been evaluated by a hydrogeologist in Region 4's Technical Services Section. The ability to capture leachate was the focus of the evaluation and the leachate capture system was found to be effective. The Final Technical Memo is attached as an addendum. These wells are closest to the source and allow the earliest warning signal that downgradient wells may be affected. Since the recent NIMS and MATT comparison demonstrate that the perimeter wells do not pose a risk and the monitoring wells act as an effective early warning signal, it is unnecessary to obtain additional groundwater samples from locations beyond the perimeter well system.

Attachments (6)

1. Hercules, Inc., March 2005 Data Package for 009 Landfill using NIMS

2. A Re-analysis of the European MATT (2000) Toxicity Data and Development of a Reference Dose for Weathered Toxaphene (DRAFT)

3. Differences between Cancer and Non-Cancer Risk Assessment using Toxaphene as an example

4. October/December 2003 Technical Memos from SRTSB/TSS describing sufficiency of the monitoring wells to detect migration

5. Cover Memo and Complete Comments from SESD

6. Cover Memo and Complete Comments from OEA

cc w/o attachments:
    Winston A. Smith, Region 4 WD
    Franklin Hill, Region 4 WD
    Scott Sudweeks, Region 4 WD
    Ted Simon, Region 4 WD
    Kay Wischkaemper, Region 4 WD
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    David Lopez, OSWER/OERR
    Silvina Fonseca, OSWER/OERR

OIG Technical Comments on the Region 4 Response

OIG Draft Recommendation 2.1:

"Use negative ion mass spectroscopy to definitely determine if toxaphene breakdown products are present in the surrounding groundwater at the Hercules 009 Landfill site, and (if so) in what amounts."

OIG Technical Comments on Region 4's Response:

The groundwater at the Hercules 009 Landfill was recently analyzed using negative ion mass spectroscopy (NIMS). In March 2005, Hercules Incorporated voluntarily collected an additional set of groundwater samples from the Hercules 009 Landfill's monitoring wells. These samples were subsequently analyzed by EnChem using Method 8081A and also by Keith Maruya from the Skidaway Institute of Oceanography using a NIMS methodology. EnChem found no measurable concentration of chlorinated camphene in monitoring well N-11. Skidaway found an estimated concentration of 0.74 μg/L (a.k.a. parts per billion, or ppb) of chlorinated camphene in monitoring well N-11. Thus, all reported chlorinated camphene values from EnChem and Skidaway were below the level of concern of 3.0 μg/L for technical toxaphene.

The OIG's review of the scientific literature regarding toxaphene found several sources that identified potential problems with analyzing for toxaphene degradation products. The Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Toxaphene reported that sulfuric acid cleanup of toxaphene sample extracts modify the toxaphene peak profile (ATSDR, 1996, p. 147). This suggests that the sulfuric acid cleanup procedure has the potential to destroy or alter the ratio of toxaphene degradation congeners. In 1997, Alder reported that gas chromatograph injector temperatures greater than 240° C have been observed to decompose or to decrease the observed response of the toxaphene congeners p50 and p62 prior to their measurement by the detector (Alder 1997). In 1995, Andrews found during a round-robin study on the analysis of toxaphene that only 15 to 30 percent of the toxaphene components were eluted from the silica or florisil columns with a nonpolar solvent (Andrews 1995). These observations indicate that the analysis for toxaphene degradation products is difficult and the analytical results can vary significantly depending on how the analysis was conducted.

The case narrative for the March 2005 Hercules 009 Landfill data from both EnChem and Skidway indicated that sulfuric acid was used to cleanup the extracts and that the gas chromatograph injector temperature may have been as high as 250° C. The OIG is concerned that the sulfuric acid cleanup and that the gas chromatograph injector temperature, if it exceeded 240° C, may have lowered the amount of chlorinated camphene detected.

Following OIG discussions with Region 4 concerning these procedural issues with the method, Region 4 provided additional test results from Region 4's Science and Ecosystem Support Division (SESD). For their analyses, the sample extracts were not subjected to sulfuric acid cleanup and the gas chromatograph injector temperature was known to be below 240° C. In data dated November 28, 2004, and January 13, 2005, SESD reported chlorinated camphene sample results for monitoring well N-11 of 4.0 JN µg/L and 6.4 JN µg/L, respectively. These results are significantly higher than Enchem's and Skidaway's chlorinated camphene results. SESD's chlorinated camphene results of 6.4 µg/L for monitoring well N-11 are 8.6 times greater than Skidaway's chlorinated camphene results of 0.74 µg/L. SESD's reported chlorinated camphene results are above the level of concern of 3.0 µg/L for technical toxaphene.

These results for chlorinated camphene show that the analysis of toxaphene is a complicated process in which the type and skill used in the extraction, cleanup, and testing procedures can directly impact the reported analytical results. To verify and document that all analytical variables are under control, a laboratory normally analyzes a spiked laboratory quality control sample (i.e., positive control sample) to confirm that the laboratory's processing of the sample extract did not destory or lose the compound(s) of interest (i.e., Hx-Sed, Hp-Sed, p26, and p50). Instead, all three laboratories (i.e., EnChem, Skidaway, and SESD) spiked the laboratory quality control sample with technical toxaphene. This quality control procedure demonstrates the performance of the method used adequately detects and measures technical toxpahene, but does not demonstrate the method's performance on individual toxaphene congeners. To document how well the method performs with the individual congeners of interest, such as Hx-Sed, Hp-Sed, p26, and p50, the laboratories needed to spike and measure the recoveries for the individual toxaphene degradation products (i.e., Hx-Sed, Hp-Sed, p26, and p50) and not technical toxaphene.

An example of this congener-specific quality control spiked sample can be seen in Foreid's 2000 paper referenced by Keith Maruya's letter dated August 4, 2005 (Foreid 2000). Foreid specifically spikes p26, p50, and p62 and demonstrates spiked sample recoveries for each congener of greater than 94 percent. These quality control results clearly demonstrated that the specific silica fractionation and sulphuric acid cleanup procedure used by Foreid did not destroy or degrade the toxaphene congeners of interest. This type of quality control results on individual congeners would have greatly assisted in interpreting the EnChem, Skidaway, and SESD results from the Hercules 009 Landfill. Unfortunately, this type of quality control results were unavailable for the Hercules 009 Landfill data because there is no standardized, validated, or EPA approved method to analyze for toxaphene degradation products. The OIG believes that spiked sample recoveries of the individual toxaphene congeners of interest, such as Hx-Sed, Hp-Sed, p26, p50, and p62, should be incorporated into any NIMS method considered by the EPA for developing and validating.

The OIG agrees with Region 4 that developing and validating a NIMS method for toxaphene congeners needs to be initiated and supported at the national program office level. Due to the degraded nature of the remaining toxaphene contamination left in the environment (i.e., a substantial amount due to the bulk use of toxaphene over many years), the NIMS method is needed by the EPA to accurately determine the extent of the remaining contamination in the environment and to provide toxicologically-relevant analytical data for assessing the risk to human health from these remaining toxaphene breakdown congeners. Therefore, future groundwater monitoring at the Hercules 009 Landfill should use, if developed and validated, the EPA-approved NIMS method.

The OIG disagrees with the statement in the Hercules Incorporated cover letter dated April 11, 2005, that "... the ECD-NCIMS method is essentially the same as Method 2 (Total Area Under the Curve)...". The NIMS method has the ability to positively identify the presence of individual toxaphene congeners and to measure the concentration of individual toxaphene congeners, while Method 2 can not. Method 2 does not provide congener specific information on toxaphene that is needed to evaluate the risk to humans from the potential exposure to the persistent toxaphene degradation congeners. Thus, these two analytical methods are not "essentially" the same.

OIG Draft Recommendation 2.2:

"If toxaphene breakdown products are found in the groundwater, assess the resulting risk to human health and take appropriate action"

OIG Technical Comments on Region 4's Response:

Regarding assessing the toxicity of toxaphene, since humans are exposed to toxaphene degradation products (e.g., mainly p26 and p50) and since individual congeners can have dramatically different toxicities, the toxicity criteria for weathered toxaphene must be developed and used. The OIG believes that the toxicity criteria for technical toxaphene should not be used, because the public is no longer exposed to the original mixture of toxaphene congeners.

Regarding a critical toxic endpoint, the OIG agrees with Region 4 that weathered toxaphene acts as a tumor promoter and not as a tumor initiator (i.e., causing direct damage to deoxyribonucleic acid, also known as DNA). The OIG also agrees with Region 4 that the use of the reference dose represents one of the first instances in which EPA has applied a threshold-type toxicity to a potentially carcinogenic compound. Due to the novelty of the application under the EPA's new cancer guideline, developing a reference dose for weathered toxaphene needs to be peer-reviewed and a consensus reached both internal and external to the EPA before a threshold limit for expose to toxaphene degradation products can be set and used for risk assessment.

Region 4's response stated that the MATT study conducted by the European Union is the sole information on the toxicity of weathered toxaphene. However, Region 4's response indicated that the MATT study may have some technical and conceptual issues that a pending peer review may elucidate. The MATT study does not clarify the mode of action as to whether the ultimate carcinogen is from the persistent congeners or from non-persistent congeners. Therefore, the OIG believes that the MATT study results alone do not provide sufficiently robust toxicity data to support setting a threshold limit for weathered toxaphene. Consequently, the OIG believes additional research is needed to characterize and assess the mode of action of the toxaphene degradation products to generate a sufficient quantity and of high-quality toxicity data on weathered toxaphene to support a threshold limit. The OIG agrees with Region 4 that additional research should focus on the toxicity of the persistent toxaphene degradation products, namely, p26 and p50, but also the less abundant products p62, p 40, p41, and p44, because they are most likely to produce the toxic effects.

OIG Draft Recommendation 3.1:

"Issue the report on the Hercules 009 Landfill 5-year review with the conclusion that the protectiveness of the groundwater cleanup cannot be determined at this time, and further evaluation is needed. A timeframe should be estimated for such an evaluation."

OIG Technical Comments on Region 4's Response:

The Ombudsman contends that the 5-year review can be issued stating that the cleanup of the Hercules 009 Landfill protects human health for the following reasons:

- The OIG observed a reoccurring pattern in the Hercules 009 Landfill groundwater monitoring data from 2002, 2004, and 2005. The analytical results from monitoring wells N-06SR and N-11 suggest that toxaphene degradation products (i.e., measured as chlorinated camphenes) are present and may exceed the 3.0 µg/L level of concern for technical toxaphene at these locations. Monitoring wells N-06SR and N-11 always had the highest observed concentrations of chlorinated camphenes during each individual sampling event. By contrast, the analytical results from the remaining monitoring wells for the site, many of which are down gradient of wells N-06SR and N-11, suggest that the toxaphene degradation products in the groundwater have not left the Hercules 009 Landfill property. Thus, the surrounding community is not being exposed to toxaphene degradation products through the groundwater exposure pathway.
- No groundwater wells are being used in the vicinity of the Hercules 009 Landfill.
- Although a deed restriction was not placed on the Hercules 009 Landfill property to prevent drilling and using wells on the property in the future, the consent decree was recorded in the records of Glynn County.

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Appendix D

Distribution

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 31 2006

OFFICE OF
INSPECTOR GENERAL

MEMORANDUM

SUBJECT: OIG Ombudsman Report 2005-P-00022
Appropriate Testing and Timely Reporting Are Needed at the
Hercules 009 Landfill Superfund Site, Brunswick, Georgia

FROM: Paul D. McKechnie Paul D. McKechnie
Director of Public Liaison
Office of Congressional and Public Liaison

TO: J. I. Palmer, Jr.
Regional Administrator
Region 4

We have evaluated your final response dated June 20, 2006, to the subject report, as well as the related attachments (such as the second 5-year report dated June 2006) and additional documents provided by members of your staff. The latter included the article by Ted Simon and Randall Manning, *Development of a reference dose for the persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion,* and the results of recent tests of the groundwater at the Hercules 009 Landfill site. The associated documents were reviewed by a chemist currently on our staff and by the subject matter expert who worked on the assignment who is now employed by another Federal agency. We also took into consideration the comments provided to us on September 7 and October 10, 2006, by the Glynn Environmental Coalition and its consultants.

We believe additional research is necessary to increase the confidence in Region IV's assessment on the human health risks posed by toxaphene degradation products, however, we are closing this report because you have adequately addressed the recommendations we made. Our basis for reaching this conclusion is described in the attached letter dated October 23, 2006. As this letter points out, for scientific and regulatory transparency, you should provide a detailed description of how the preliminary remediation goals (PRGs) for weathered toxaphene were calculated. Some other key points related to your response that are detailed in the letter are:

- The PRGs Region IV developed for weathered toxaphene, not the drinking water program's maximum contaminant level for technical toxaphene, should now be used to evaluate the human health risk.

- When toxaphene contamination is suspected, the groundwater and soil analyses should test for Hx-Sed and Hp-Sed because they would be the dominant toxaphene degradation products.

- The analysis performed on the groundwater samples collected at the Hercules 009 Landfill in March 2006 (not March 2005) included quality controls sufficient to ensure the results can be accurately interpreted.

As we noted in Report 2006-P-00007 dated December 16, 2005, *More Information Is Needed On Toxaphene Degradation Products,* additional research and scientific study is needed to assess the health risk posed by the human exposure to toxaphene degradation products. We urge you to work closely with the Office of Research and Development as they prepare their multi-year research plan, so it includes toxaphene degradation products. Similarly, we believe the Office of Research and Development and the Office of Solid Waste and Emergency Response will need help from you to develop the analytical method using negative ion mass spectroscopy.

If you or your staff has any questions regarding this matter, please contact me at 617-918-1471 or Christine Baughman, the Project Manager, at 202-566-2902.

Attachment

cc: Susan Bodine, Assistant Administrator for Solid Waste and Emergency Response
George Gray, Assistant Administrator for Research and Development
Benjamin Grumbles, Assistant Administrator for Water
Stephanie Lankford, Region 4 Audit Liaison
Johnsie Webster, OSWER Audit Liaison
Cheryl Varkalis, ORD Audit Liaison
Mike Mason, OW Audit Liaison
Laurie Dubriel, Special Assistant to the Administrator
Winston A. Smith, Director, Waste Management Division, Region 4
Leo Francendese, Remedial Project Manager, Region 4
Daniel Parshley, Project Manager, Glynn Environmental Coalition

October 31, 2006

Paul Mckechnie
Director Public Liaison/Ombudsman
Environmental Protection Agency
Office of Inspector General
Office of Congressional and Public Liaison
1200 Pennsylvania, Ave, N.W. (2491T)
Washington, D.C. 20460

Dear Paul,

At your request, I am providing you my technical opinion on EPA Region IV's final response (Dated June 20, 2006) to the Ombudsman's Recommendations 2.1 and 2.2 in the Report 2005-P-00022 (dated Sept. 26, 2005). The Ombudsman Report 2005-P-00022 concerned EPA Region IV's assessment, during the second 5-Year Review, of the public health risk posed by degraded toxaphene at the Hercules 009 Landfill Superfund site. As a former EPA/OIG Environmental Scientist on your staff, I served as the subject matter expert for each of the Ombudsman reports on toxaphene (i.e., Reports 2005-P-00022 and 2006-P-00007). This experience provides me with an in depth knowledge of the subject and I present my observations and findings for your consideration. Since I am no longer an EPA employee, this review and subsequent development of my technical opinion were performed pro bono.

I received and reviewed the following five documents to develop my technical opinion on Region IV's final response to the OIG's Recommendations 2.1 and 2.2 in Report 2005-P-00022:

- [EPA Region IV's] Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia Assignment 2004-124* (dated June 20, 2006).

- The Hercules 009 Landfill April 2006 GC/ECD and GC/ECNI-MS-SIM ground water testing results performed by Pace Analytical Laboratories on behalf of Hercules Incorporated (dated June 15, 2006).

- Ted Simon, Randall Manning; Development of a reference dose for persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion. Regulatory Toxicology and Pharmacology, Vol. 44 (2006), pages 268-281.

- Comment from the Glynn Environmental Coalition on the June 20, 2006, EPA Region 4, Final Response to the Recommendations and Final Report for the Hercules 009 Landfill OIG/Ombudsman Report *Appropriate Testing and Timely Reporting Are Needed at the Hercules 009 Landfill Superfund Site Brunswick, Georgia* (dated September 7, 2006) including the enclosed attachments from R. Kevin Pegg, Ph.D. and Kathleen Burns, Ph.D.

- Comments to OIG on Hercules 009 Superfund Reports by Jennifer Sass, Ph.D. (dated October 10, 2006).

The purpose of a 5-year review is to assess if the remedy is still protective in light of any new science or site information that has occurred since the last assessment. Since toxaphene is well known in the scientific literature to degrade in the environment, the 5-year review needs to determine the amount of exposure (if any) and the resulting risk to the public from degraded toxaphene from the site. This is accomplished by accurately measuring the amount of degraded toxaphene in the groundwater at the site, by determining if any of the contaminated toxaphene groundwater has left the site, and by determining the human health risk posed by any degraded toxaphene that might have left the site.

Evaluation of Hercules 009 Groundwater Testing

The second 5-year review of the Hercules 009 site used the Gas Chromatography/Negative Ion Mass Spectrometry (GC/NIMS) method to determine the amount of degraded toxaphene in the groundwater. However, the March 2005 GC/NIMS groundwater results have several limitations:

- The test results do not positively identify individual toxaphene degradation congeners (i.e., through a mass spectrum or selective ion monitoring confirmation) or determine the amount of individual toxaphene degradation congeners (i.e., p26, p50, Hx-Sed, Hp-Sed, etc.) present in the groundwater. This severely limits the ability to technically interpret the results with an acceptable level of confidence.

- The Quality Control used in March 2005 did not incorporate a Laboratory Control Sample (LCS) that contained known amounts of individual toxaphene degradation congeners. Therefore, without LCS results for individual congeners, the ability of the method to detect and confirm the presence of individual toxaphene congeners is questionable.

However, the GC/NIMS groundwater samples taken subsequently at the Hercules 009 Landfill site in April 2006 can be accurately interpreted. These GC/NIMS groundwater sample results are the type of testing the OIG/Ombudsman has been requesting in order to accurately measure the amount of degraded toxaphene in the groundwater at the site and to determine if any of the contaminated toxaphene groundwater has left the site.

The GC/NIMS groundwater samples taken at the Hercules 009 Landfill site in April 2006 positively identify (i.e., by Selective Ion Monitoring (SIM)) and quantitate the following eight individual toxaphene congeners: p26, p41, p40, p44, p50, p62, Hx-Sed, and Hp-Sed. In reviewing the results, the following observations and findings can be made:

- The method blank results show no laboratory contamination of toxaphene congeners.

The Laboratory Control Sample (LCS) and LCS duplicate recoveries are from 63% to 95% for the eight individual congeners and show that the GC/NIMS analysis is performing well for the detection of these eight individual toxaphene congeners. The LCS quality control results document the method's ability to detect individual toxaphene congeners in samples reliably.

- Matrix Spike (MS) and Matrix Spike Duplicate (MSD) quality control sample recoveries are from 60% to 96% for the eight individual congeners and show that the groundwater matrix does not interfere with the analysis.
- Only two groundwater monitoring wells, N-06SR and N-11, were found to have degraded toxaphene congeners significantly above the Level of Quantitation (LOQ) (See Table 1). These results are consistent with the published science on the degradation of technical toxaphene. The dominant congeners generated by the microbial breakdown of technical toxaphene are Hx-Sed and Hp-Sed with the other toxaphene congeners being present at much lower levels. The other toxaphene degradation congeners of concern (i.e., p26, p40, p41, p44, p50, and p62) would only become the dominant congeners upon the subsequent metabolism of this microbially degraded toxaphene (e.g., Hx-Sed and Hp-Sed) by higher organisms (e.g., fish or humans). The groundwater results for monitoring wells N-06SR and N-11 show that the technical toxaphene has degraded and that Hx-Sed and Hp-Sed are the dominant congeners with the other toxaphene congeners being present at much lower levels.

Ground Water Well	Hx-Sed (ppb)	Hp-Sed (ppb)	p26 (ppb)	p40 (ppb)	p41 (ppb)
N-06SR	0.186	0.128	0.009	≤0.005	0.005
N-06SR Duplicate	0.156	0.116	0.009	0.034	0.005
N-11	0.133	0.095	≤0.005	0.012	≤0.005
N-14S	≤0.005	≤0.005	≤0.005	≤0.005	<0.005
N-14D	<0.005	<0.005	<0.005	<0.005	<0.005

Table 1: Subset of the April 2006 GC/NIMS Groundwater Results

The groundwater results for the furthest down-gradient monitoring well, N-14, did not detect toxaphene degradation products above the LOQ (See Table 1). This indicates that the toxaphene degradation products found in groundwater wells N-06SR and N-11 have not left site.

OIG Recommendation 2.1

The OIG recommendation to the EPA Region IV was to use the GC/NIMS to definitively determine if toxaphene breakdown products are present in and around the surrounding groundwater at the Hercules 009 Landfill site, and (if so) in what amounts.

EPA Region 4 has implemented the OIG Recommendation 2.1 with the April 2006 GC/NIMS groundwater testing at the Hercules 009 Landfill. These groundwater results definitively show that the technical toxaphene can and has degraded and that Hx-Sed and Hp-Sed (i.e., the microbial toxaphene breakdown products) are present at a maximum concentration of 0.186 ppb and 0.128 ppb, respectively. Several of the other toxaphene congeners (e.g., p26, p40, and p41) are also present, but at much lower levels. Since the April 2006 GC/NIMS groundwater results are consistent with the published science on the degradation of technical toxaphene and since the LCS and MS quality control results indicate that the GC/NIMS method was performing well, the April 2006 GC/NIMS groundwater results can be concluded to accurately characterize the site's groundwater conditions for toxaphene degradation products.

Unfortunately, EPA Region IV and I continue to disagree as to whether environmental testing for toxaphene degradation products by the GC/NIMS methodology should include Hx-Sed and Hp-Sed. Region IV does not agree with the OIG's stated opinion that Hp-Sed and Hx-Sed congeners need to be definitively determined in environmental testing for toxaphene degradation products (see Region IV Final Response cover memo, page 2; and Attachment C of the Region IV Final Response, page 38). In my opinion, the published science is clear that the dominant congeners generated by the microbial breakdown of technical toxaphene in soil are Hx-Sed and Hp-Sed with the other toxaphene congeners being present at much lower levels. Therefore, if the EPA or the potentially responsible party (PRP) are testing to determine the nature and extent of the contamination at a site by toxaphene degradation products, the dominant toxaphene congeners in the soil or groundwater samples will be Hx-Sed and Hp-Sed. The other toxaphene degradation congeners of principal concern for the human health evaluation (e.g., p26, p50, and p62) would only become the dominant congeners upon the subsequent metabolism of this microbially degraded toxaphene (e.g., Hx-Sed and Hp-Sed) by higher organisms (e.g., fish or humans). Therefore, if the EPA or PRP test a site for only the p26, p50, and p62 congeners, the EPA or PRP will significantly under estimate the amount of contamination by ~~toxaphene degradation products at the site.~~

Furthermore, the EPA and/or the PRP need to monitor the groundwater at a site to insure that toxaphene contaminated groundwater is not leaving the site. Since Hx-Sed and Hp-Sed would be the dominant congeners in groundwater, how can EPA or the PRP monitor the groundwater contamination and determine if the contamination is leaving the site without monitoring for Hx-Sed and Hp-Sed? Furthermore, the additional cost to test for the Hx-Sed and Hp-Sed congeners in the GC/NIMS method is minimal (i.e., the cost of including the Hx-Sed and Hp-Sed in the calibration standards and spike solutions for the LCS and MS quality control samples). There is no practical or scientific reason to exclude Hx-Sed and Hp-Sed in the testing for contamination by toxaphene degradation products. Therefore, it is my opinion that it is imperative that the EPA-approved GC/NIMS method under development by the Office of Research and Development include Hx-Sed and Hp-Sed as target congeners in the method.

Evaluation of the Human Health Risk to Degraded Toxaphene

EPA Region IV Final Response (Cover Memo) compares the concentrations of toxaphene degradation products in the groundwater to the drinking water maximum contaminant level (MCL) of 3.0 ppb for technical toxaphene. The composition of the congeners present in technical toxaphene is distinctly different than the composition of the congeners found in degraded toxaphene. The composition of technical toxaphene is mostly comprised of the higher chlorinated level of boranes, while the degraded toxaphene is principally made of the lower chlorinated levels of boranes such as Hx-Sed, Hp-Sed, p26, p50 and p62, etc. Furthermore, since the last significant use of technical toxaphene was in 1982 and since technical toxaphene is known to degrade in the environment, the human population is no longer exposed to technical toxaphene, but is exposed to toxaphene degradation products. Therefore, the continued application of the drinking water MCL of 3.0 ppb for technical toxaphene in the risk assessment of toxaphene degradation products is scientifically inappropriate. For that matter, since the human population is and will no longer be exposed to technical toxaphene, the drinking water MCL of 3.0 ppb for technical toxaphene can be retired for the lack of an appropriate risk management application.

In response to the OIG Recommendation 2.2 to assess the risk to human health from the potential exposure to toxaphene breakdown products, EPA Region IV conducted a re-analysis of the European MATT (2000) toxicity data and developed a reference dose for weathered toxaphene. Ted Simon and Randall Manning published their findings in the following scientific journal: Regulatory Toxicology and Pharmacology, Vol. 44 (2006), pages 268-281. EPA Region IV states in their Final Response (See attachment B, page 2) that "… the Simon/Manning approach should be considered the best available science; therefore, the Region's reliance on this approach to assess the risk associated with this site is appropriate."

In my opinion, the Simon and Manning paper is significant in the field of scientific research into toxaphene because it is the first published paper that quantifies the risk of weathered toxaphene. The authors make a number of key determinations (e.g., weathered toxaphene's mode of action is as a promoter, applied the unconventional use of a reference dose to a carcinogen, applied a uncertainty factor of a 100, etc.) whose application for calculating an acceptable exposure limit to weathered toxaphene is open for debate and to further research and study within the scientific community. However, the Simon/Manning paper does represent the best and only available scientific information that quantifies the human health risk to weathered toxaphene for use in the second 5-year review of the Hercules 009 Landfill. Science is dynamic and continuously evolves as new information becomes available, so the Simon/Manning paper is not the last word on the issue, but represents the next step into the understanding of the amount of risk posed by weathered toxaphene. More scientific information should be available in five years to allow for a better estimate of the human health risk posed by weathered toxaphene for the next 5-review of the Hercules 009 Landfill in 2011.

EPA Region IV states in their Final Response (See attachment B, page 2) that "… the Simon/Manning approach should be considered the best available science; therefore, the Region's reliance on this approach to assess the risk associated with this site is appropriate." However, EPA Region IV does not use the Simon/Manning approach to assess the risk associated with this site. EPA compares the concentrations of toxaphene congeners in the groundwater to the drinking water MCL of 3.0 ppb. However, in my opinion, to be consistent with their statement on the Simon/Manning approach, EPA Region IV needs to evaluate the concentrations of toxaphene degradation products against the Preliminary Remediation Goals (PRGs) established in the Simon/Manning paper for ∑3PC and weather toxaphene of 0.03 ug/L and 0.6 ug/L, respectively (See Table 5 in the Simon and Manning paper). Unfortunately, the Simon/Manning paper does not show how the PRGs were calculated. Therefore, I cannot independently verify them (i.e., EPA Region IV should be required to provide a detailed description of how these PRGs were calculated for scientific and regulatory transparency). However, EPA Region IV clearly states that it is the "best available science." Thus, EPA Region IV should apply these PRGs to the assessment of the risks associated with weathered toxaphene at the Hercules 009 Landfill and other toxaphene contaminated Superfund sites in Region IV. In other words, the EPA Region IV should use the 0.6 ug/L PRG for weathered toxaphene (which is 5-fold more restrictive than the 3.0 ppb drinking water MCL being applied by the Region) to evaluate the concentrations of degraded toxaphene congeners found in the groundwater.

When the April 2006 GC/NIMS groundwater results for the Hercules 009 Landfill site are compared against the PRGs for ∑3PC and for weathered toxaphene, the concentration of the toxaphene degradation products do not exceed either PRG. The groundwater samples from monitoring well N-06SR contained the highest levels of toxaphene degradation products. Specifically, the groundwater sample and duplicate from N-06SR contained 0.328 ug/L and 0.320 ug/L of weathered toxaphene, respectively. Both results are below the 0.6 ug/L PRG for weathered toxaphene. Furthermore, the groundwater sample and duplicate from N-06SR contained 0.009 ug/L and 0.009 ug/L for ∑3PC, respectively. Both results are below the 0.030 ug/L PRG for ∑3PC. Therefore, the level of groundwater contamination by toxaphene degradation products at the Hercules 009 Landfill site does not exceed the preliminary remediation goals and does not pose a health risk to the community at these levels

OIG Recommendation 2.2

The OIG recommendation to the EPA Region IV was to assess the risk to human health by exposure to toxaphene breakdown products.

EPA Region IV has met the OIG Recommendation 2.2 with the development and publication of the Simon and Manning paper and their development of the Preliminary Remediation Goals for ∑3PC and Weathered Toxaphene of 0.03 ug/L and 0.6 ug/L, respectively (See Table 5 in the Simon and Manning paper). However, the EPA Region IV should be required to provide a detailed description of how these PRGs were calculated for scientific and regulatory transparency.

Protectiveness Statement

Based on the April 2006 GC/NIMS groundwater results indicating that the toxaphene degradation products have not left the site through the groundwater and also based on the observation that the maximum concentration of toxaphene degradation products is below the PRGs for ∑3PC and weather toxaphene of 0.03 ug/L and 0.6 ug/L, respectively, I concur with the Regional findings of the second 5-year review that the Hercules 009 Landfill site remedy is protective of human health and the potential exposure pathways are under control in regard to the contaminant toxaphene and its degradation products.

Conclusion

The two Ombudsman reports on toxaphene have been influential in shifting the entrenched paradigm of the EPA and PRPs to perpetually test for technical toxaphene and subsequently evaluate the risk against the limits set for technical toxaphene. The Ombudsman's efforts have promoted the recognition that currently, toxaphene only exists in the environment in a degraded, weathered state and that the regulatory and scientific communities need to test for and assess the risk posed from human exposure to weathered toxaphene. Furthermore, the completion of the EPA-approved GC/NIMS method by the end of 2008 and the subsequent use of this method by EPA and PRPs will definitively determine the extent of degraded toxaphene contamination left in the environment from 32 years of heavy use as an insecticide.

Sincerely,

/s/
Michael Wilson
Former Environmental Scientist with the EPA/OIG

cc: Christine Baughman

OFFICE OF INSPECTOR GENERAL

Catalyst for Improving the Environment

Ombudsman Report

More Information Is Needed On Toxaphene Degradation Products

Report No. 2006-P-00007

December 16, 2005

Report Contributors:

Christine Baughman
Tapati Bhattacharyya
Stephen Schanamann
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Abbreviations

CLE	Cod liver extract
DDT/DDE	Dichlorodiphenyltrichloroethane and its metabolic byproduct, DDE
EPA	U.S. Environmental Protection Agency
GA/DNR	Georgia Department of Natural Resources
GC/ECD	Gas chromatography with electron capture detector
HCH	Halogenated hydrocarbons
IRIS	Integrated Risk Information System
MATT	Investigation into the Monitoring, Analysis, and Toxicity of Toxaphene
MCL	Maximum containment level
MNA	Monitored natural attenuation
NIMS	Gas chromatography with negative ion mass spectroscopy
NPDWR	National Primary Drinking Water Regulations
OIG	Office of Inspector General
PCB	Polychlorinated biphenyl
ppb	Parts per billion
ppt	Parts per trillion
PWS	Public water system
RfD	Reference dose
SW-846	Test Methods for Evaluating Solid Waste, Physical/Chemical Methods
TCDD	Tetrachlorodibenzo-*p*-dioxin
TDI	Tolerable daily intake
ug/L	Micrograms per liter

Cover photo: An airplane applying pesticides to a field.

U.S. Environmental Protection Agency
Office of Inspector General

2006-P-00007
December 16, 2005

At a Glance

Catalyst for Improving the Environment

Why We Did This Review

The Glynn Environmental Coalition, a nonprofit community organization, brought to the Ombudsman's attention concerns about toxaphene at a Superfund site in Georgia.

Background

Toxaphene is an agricultural pesticide that was heavily used in the United States during the 1960s and 1970s. EPA banned it for most uses in 1982, and for all uses in 1990, because it posed a risk of significant adverse impacts on humans and the environment. To further protect people from the effects of toxaphene, EPA limited how much toxaphene can be in drinking water and required related monitoring. The EPA Superfund program is cleaning up numerous sites contaminated with toxaphene.

For further information, contact our Office of Congressional and Public Liaison at (202) 566-2391.

To view the full report, click on the following link:

www.epa.gov/oig/reports/2006/20051216-2006-P-00007.pdf

More Information Is Needed On Toxaphene Degradation Products

What We Found

Toxaphene in the environment changes, or degrades. The resulting degradation products are different from the original toxaphene in chemical composition and how they appear to testing instruments, so they could go unreported. The analytical methods EPA uses to identify and measure toxaphene are not designed to identify toxaphene degradation products. However, a new testing method used by others specifically tests for toxaphene degradation products. We believe EPA should validate, approve, and use this method.

Certain toxaphene degradation products accumulate inside people. Although studies indicate that some of these degradation products may be harmful, more research is needed to determine how much of a risk these products pose to people.

What We Recommend

We recommend that the EPA Administrator direct

- The Assistant Administrators for Water and for Solid Waste and Emergency Response to validate and approve the new analytical method that tests for toxaphene degradation products, and use the new method to analyze environmental samples.

- The Assistant Administrator for Research and Development to work with others in EPA to arrange for the specific research needed to determine the risk that toxaphene degradation products may pose to people.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

THE INSPECTOR GENERAL

December 16, 2005

MEMORANDUM

SUBJECT: More Information Is Needed On Toxaphene Degradation Products
Report No. 2006-P-00007

TO: Stephen L. Johnson
Administrator

This is our final report on a review of toxaphene conducted by the Office of Inspector General (OIG) of the U.S. Environmental Protection Agency (EPA). This report contains findings that describe the problems the OIG has identified and corrective action the OIG recommends. This report represents the opinion of the OIG and the findings contained in this report do not necessarily represent the final EPA position. Final determinations on matters in this report will be made by EPA managers in accordance with established resolution procedures.

Action Required

In accordance with EPA Manual 2750, you are required to provide a written response to this report within 90 calendar days of the date of this report. You should include a corrective action plan for agreed upon actions, including milestone dates. We have no objection to the further release of this report to the public. For your convenience, this report will be available at http://www.epa.gov/oig/publications.htm.

If you or your staff have any questions regarding this report, please contact me at 202-566-0847 or Eileen McMahon, the Assistant Inspector General for Congressional and Public Liaison, at 202-566-2546.

Nikki L. Tinsley
Nikki L. Tinsley

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Chapter 1
Introduction

Purpose

The purpose of this report is to bring issues related to toxaphene, an agricultural pesticide, to the attention of EPA management. The issues about toxaphene stem from a complaint made by the Glynn Environmental Coalition (a nonprofit community organization) to the Ombudsman at the U.S. Environmental Protection Agency's (EPA's) Office of Inspector General (OIG). The OIG Ombudsman reviews and reports on public concerns regarding EPA activities, including Superfund, which is the EPA program to clean up uncontrolled hazardous waste sites. The complaint pertained to toxaphene found at the Hercules 009 Landfill Superfund site in Georgia, in EPA Region 4. We have issued a separate report to the Regional Administrator of Region 4 recommending appropriate actions regarding the Hercules 009 Landfill (Report No. 2005-P-00022, September 26, 2005). However, since we found that the issues related to toxaphene were broader than just that site, we believe EPA needs to address them nationwide.

Background Information

Toxaphene first became available commercially in 1948. Toxaphene came in various forms and was used against insect pests of cotton, tobacco, forests, turf, ornamental plants, grains, vegetables, and livestock. It was also used in the 1950s and early 1960s by fisheries in several States to remove unwanted fish from lakes and ponds. This use was discontinued or prohibited when unexpectedly high amounts remained in some lakes. During the 1960s and 1970s, it was the most heavily used pesticide in the United States, with the southern United States and California using it the most.

Toxaphene poses a risk of significant adverse impacts on humans and the environment. If people breathe, eat, or drink large amounts of toxaphene, it may damage the lungs, nervous system, and kidneys, and can even cause death. Consequently, with a few exceptions, EPA cancelled the registrations for all uses of toxaphene in November 1982. A registration is a license allowing a pesticide product to be sold and distributed for specific uses in accordance with specific use instructions, precautions, and other terms and conditions. Although most of the existing stocks of cancelled products had to be sold and used before 1984, some could be sold and used according to label specifications through 1986. EPA banned all uses of toxaphene in 1990.

Although toxaphene can no longer be used, some remains in the environment. People must be protected from its effects. Therefore, under the Safe Drinking Water Act, EPA set a limit on the amount of toxaphene that can be in the drinking water: the limit is 0.003 milligrams per liter. As a result, public water systems must monitor the level of toxaphene in their drinking water. Also because of health risks associated with toxaphene, various States have issued a total of 25 advisories that people not eat fish from 10 locations around the country. Toxaphene was identified as a contaminant of concern in at least 16 Superfund sites; these sites, most of which are located in the southeastern part of the United States, are identified in Appendix B. Other information indicates toxaphene has been found in as many as 58 Superfund sites.

When toxaphene is released in the environment, it transforms into substances known as toxaphene degradation products that may be harmful to human health. The extent of the health risk depends on the amount of degradation products to which people are exposed, and the types of danger the substances pose. Therefore, to assess the potential human health risk associated with toxaphene degradation products, information on both amounts and dangers is needed. Chapter 2 of this report addresses (1) identifying and measuring toxaphene degradation products to determine exposure, and (2) potential dangers. Appendix A contains a technical discussion of these matters.

Scope and Methodology

We began field work on this review in June 2004 and completed it in January 2005. During that period, we interviewed EPA officials in Region 4, the Office of Solid Waste and Emergency Response, and the Office of Research and Development. We also met with representatives of the Glynn Environmental Coalition, U.S. Army Corps of Engineers, and the Skidaway Institute of Oceanography. The OIG team reviewed toxaphene testing protocols and about 50 journal articles on toxicity and exposure issues related to toxaphene, and obtained additional information from various Federal Internet sites.

On August 12, 2005, the OIG issued a draft report to the EPA Administrator for review and comment. The Deputy Administrator responded on September 26, 2005. This response, which included comments from the Office of Research and Development, Office of Solid Waste and Emergency Response, and Office of Water, stated that EPA generally concurred with the recommendations. They suggested some specific changes to the report. As appropriate, we revised the report based on their comments. We provide a summary and general evaluation of the EPA comments and our response at the end of Chapter 2. We included the Deputy Administrator's memorandum in Appendix C. Appendix D is the OIG evaluation of the technical aspects of the EPA response.

We performed our review in accordance with *Government Auditing Standards* issued by the Comptroller General of the United States. However, our review of management controls and compliance was limited to those directly related to the issue under review.

The findings in this report are not binding in any enforcement proceedings brought by EPA or the Department of Justice under the Comprehensive Environmental Response, Compensation, and Liability Act to recover costs incurred not inconsistent with the National Contingency Plan.

Chapter 2

Exposure and Risk Information about Toxaphene Degradation Products Is Needed

Exposure and risk information is necessary to complete a risk assessment of the toxaphene degradation products that result when toxaphene is released into the environment. A few studies indicate these degradation products may pose a danger to human health, but more research on the risks is needed. To determine exposure, an analytical method that identifies and measures toxaphene degradation products is required. One is available, but needs to be approved by EPA for use in its programs.

Toxaphene Degrades in the Environment

Toxaphene was a mixture of many organic chemicals that, when released into the environment, slowly changed. The original toxaphene was produced by the chlorination of camphene, resulting in a mixture of more than 200 compounds, mostly polychlorinated camphenes and bornanes. Generally, from six to nine chlorines were attached to the camphenes and bornanes, and the average chlorine content was 67 to 69 percent

In the environment, the original toxaphene mixture dechlorinates; it breaks down (or degrades) and the components lose chlorines. It degrades with or without air present. Exactly what happens to it in the environment depends on the situation. For example, microbes in the soil are known to break down the original toxaphene into two major degradation products (i.e., Hx-Sed and Hp-Sed) and several minor degradation products. Some of the less abundant degradation products identified in soil include p26, p40, p41, p44, and p50. These degradation products are a different mixture than the original toxaphene mixture, so they appear different to the testing instruments.

Some Degradation Products Accumulate in Humans

Toxaphene degradation products can be detected in human blood, urine, breast milk, and body tissues. Toxaphene or toxaphene degradation products generally get into the body through eating fish or drinking water contaminated with these substances. Babies may be exposed if they are breast fed and the mother had been exposed. The body processes (i.e., metabolizes) these substances and most of them leave the body. Hx-Sed and Hp-Sed are examples of degradation products that quickly leave the body. However, some of the degradation products stay in the body; they accumulate or build up. These include p26, p40, p41, p44, p50, and p62. Because these degradation products accumulate in the body, they may pose a continuing risk to the person.

Studies Indicate Degradation Products May Pose a Risk

EPA was aware of the potential danger of toxaphene degradation products when it banned toxaphene. However, specifics were not known concerning which of the degradation products posed the danger and how much danger they posed. EPA's September 1986 Ambient Aquatic Life Water Quality Criteria for Toxaphene noted:

> *The compositional changes that occur in the field probably also mean that field toxicity differs to some unknown extent from toxicity determined in laboratory tests using technical-grade toxaphene. Using mice, houseflies, and goldfish, Khalifa et al. (1974), Saleh et al. (1977), and Turner et al. (1975, 1977) demonstrated that different toxaphene components have substantially different toxicities. Toxaphene that had "weathered" for 10 months in a lake was altered chemically (diminution of late eluting peaks) and was somewhat less toxic to fish than the original formulation (Lee et al. 1977). In contrast, Harder et al. (1983) found that sediment-degraded products of toxaphene were more toxic than the parent material to some saltwater fishes.*

In recent years, new scientific data have emerged on the dangers posed by ~~toxaphene degradation products that accumulate in a person, such as p26, p50,~~ and p62. A 1997 study showed that p26 and p50 caused more abnormalities in the central nervous systems of rat embryos than toxaphene caused. Another study showed that a cod liver extract containing three toxaphene degradation products (p26, p50, and p62) promoted the growth of tumors more than the original toxaphene mixture. However, the quality of this study has not been evaluated and an EPA toxicologist in Region 4 is concerned that the authors of the study erred in their interpretations.

More Studies Are Needed

More scientific data are needed on the dangers posed by toxaphene degradation products. Since the continuing risk to humans is limited to the degradation products that accumulate in the body, future studies should center principally on p26, p40, p41, p44, p50, and p62. Hx-Sed and Hp-Sed should also be considered for study because, although they do not accumulate in people, they generally occur in larger amounts. Further, the studies should address the likelihood that these degradation products will cause tumors (i.e., cancer) or will harm embryos.

The EPA Office of Research and Development has already funded some studies related to toxaphene degradation products. EPA program offices would need to provide funds to support additional studies. Such studies should be of interest to EPA's Office of Water and Office of Solid Waste and Emergency Response because, if studies show toxaphene degradation products pose a danger to human health, their programs would need to address the dangers by developing acceptable human exposure limits to mixtures of the substances. Further, until more is known, EPA will be unable to definitively determine if the cleanup of Superfund sites contaminated with toxaphene (such as the Hercules 009 Landfill) protect human health and the environment. In responding to the draft OIG report on the Hercules 009 Landfill, Region 4 agreed that additional toxicity studies of toxaphene degradation products may be helpful.

Degradation Products Should Be Monitored

Since toxaphene degradation products may pose a risk to human health, they should be monitored in the environment to obtain exposure information. As noted above, exposure information is necessary to perform a risk assessment. The ability to identify and measure toxaphene degradation products should be used by various EPA programs. Specifically, toxaphene degradation products should be targeted for analysis at toxaphene-containing sites (e.g., Superfund sites) or in toxaphene-containing media (e.g., water).

For a site to become part of the Superfund program, evidence must exist that a hazardous substance was released from the site. Under EPA's November 1992 Hazard Ranking System Guidance Manual, this evidence could include breakdown (or transformation) products. Also under the Superfund and other programs, according to EPA's April 1999 Use of Monitored Natural Attenuation at Superfund, RCRA Corrective Action, and Underground Storage Tank Sites, if a site has contaminants that are being allowed to naturally degrade (or attenuate), then monitoring should identify any potentially toxic and/or mobile transformation products. Similarly, drinking water must be monitored for contaminants with established standards, and for contaminants for which EPA may want to establish standards.

A Different Analytical Method is Needed to Identify Degradation Products

The analytical methods approved by EPA to identify and measure toxaphene do not evaluate toxaphene degradation products. The approved methods generally use a testing instrument called a gas chromatograph with electron capture detectors, and have been proved to be capable of testing for the original toxaphene mixture, but have not been formally validated for toxaphene degradation products. However, as noted above, the toxaphene degradation products are a different mixture than the original toxaphene mixture.

A new analytical method using a gas chromatograph with negative ion mass spectroscopy (NIMS) should be used to test for toxaphene degradation products.

Academia and the European Union have successfully used the NIMS method for at least 5 years to test for toxaphene degradation products in the environment.

The NIMS method provides definitive test results because the technique generates a mass spectrum for each compound in an environmental sample. A mass spectrum is like a chemical "fingerprint." If the "fingerprint" of an unknown compound in the environmental sample matches the known "fingerprint" of the toxaphene degradation product, the resulting match of the "fingerprints" would definitively identify the presence of toxaphene degradation products. On the other hand, if the "fingerprints" do not match, then the NIMS method would definitively determine that toxaphene degradation products are not present. Therefore, the use of the NIMS method provides the certainty needed to determine whether the environment is contaminated by toxaphene degradation products.

EPA Should Approve the NIMS Method

Environmental data used to make public health decisions should generally be produced through analytical methods that have been proven (or validated) by several laboratories and approved by EPA. Both EPA's Office of Solid Waste and Emergency Response and Office of Water have established procedures for approving analytical methods used by their programs. Since EPA has not approved the NIMS method, it should be subjected to the approval process of both offices.

People or companies may ask that EPA (i.e., the Office of Water, or the Office of ~~Solid Waste in the Office of Solid Waste and Emergency Response) approve a new~~ way to prepare a sample, a new way to analyze a sample, or a variation on an existing way. Such requests can also come from within EPA. If approval of a new analytical method is requested, those requesting approval must prove that the proposed method will accurately measure the amount of the specified substance in an environmental sample. If the new method will be used nationwide, three or more different laboratories must validate the method. Following validation, those requesting approval submit a variety of information to EPA about the new or revised method, including the results from the validation process, and explain why a change is needed.

If EPA agrees that a new analytical method should be adopted nationwide, how it is approved depends on whether it is for the Office of Water or the Office of Solid Waste and Emergency Response. The Office of Water must add the new method to the *Code of Federal Regulations*. This process takes several months, including publishing a proposed rule, evaluating the resulting comments from the public, and then issuing a final rule. The Office of Solid Waste approves the new method by adding it to its manual of EPA-approved methods. The public may review proposed updates to the manual before the changes become part of the manual.

Recommendations

1. We recommend that the Administrator direct the Assistant Administrators for Water and for Solid Waste and Emergency Response to:
    a. Develop, validate, and approve the gas chromatograph with negative ion mass spectroscopy method to analyze toxaphene degradation products, especially p26, p40, p41, p44, p50, p62, Hx-Sed, and Hp-Sed; and
    b. Use the gas chromatograph with negative ion mass spectroscopy method to analyze for toxaphene degradation products during sampling and testing at sites known to contain toxaphene, or whenever monitoring for toxaphene contamination.
2. We recommend that the Administrator direct the Assistant Administrators for Research and Development, for Water, and for Solid Waste and Emergency Response to arrange for specific research into the dangers of tumors (i.e., cancer) and of harm to embryos posed principally by a mixture of toxaphene congeners and metabolites found in fish.

Agency Comments and OIG Evaluation

In a memorandum dated September 26, 2005, the Deputy Administrator provided comments on the draft report from the Office of Research and Development, ~~Office of Solid Waste and Emergency Response (both the Superfund program~~ staff and solid waste program staff), and the Office of Water. In general, EPA officials concurred with the recommendations. The Deputy Administrator's memorandum is Appendix C.

The OIG's technical evaluation of the EPA response is Appendix D. In summary, we changed recommendation 1b in a manner similar to that suggested by the Office of Solid Waste. We also changed recommendation 2 as requested by the Office of Research and Development. Finally, based on the response from the Office of Water, we believe that Office has not fully appreciated the impact toxaphene degradation products may make on the National Primary Drinking Water Regulations.

Appendix A

Technical Discussion on Toxaphene

The original toxaphene pesticide mixture is known to degrade in the environment, so its degradation products may be present at Superfund sites (such as the Hercules 009 Landfill in Georgia) or in the drinking water. However, the analytical methods approved by EPA will detect and measure toxaphene, but not toxaphene degradation products. Therefore, EPA needs to use a different analytical method, such as gas chromatography with negative ion mass spectroscopy, to definitively determine if toxaphene degradation products are present in the environment and the food chain. Also, there are indications that some of the toxaphene degradation products may be at least as toxic as the original toxaphene. To assess the health risks these degradation products may pose to humans, research is needed on their carcinogenicity and embryotoxicity.

Basics of Toxaphene Chemistry

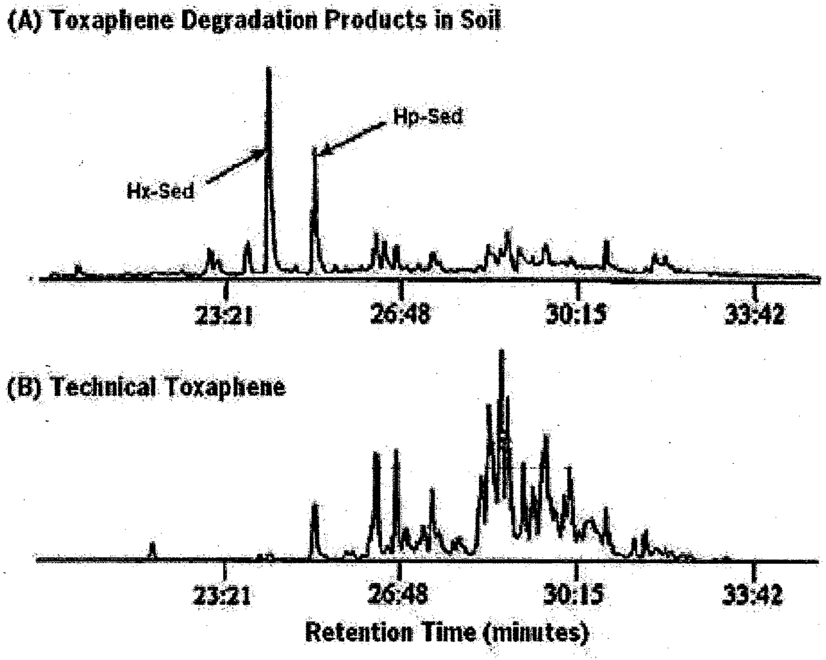
A basic understanding of the chemical structure of toxaphene is needed to address the issue. Unlike most organic environmental pollutants, toxaphene is not a single organic compound. As manufactured, the original toxaphene pesticide is a mixture of more than 200 closely related chlorinated organic compounds. This original toxaphene pesticide mixture is commonly known as "technical" toxaphene. Technical toxaphene consists mainly of polychlorinated bornanes with six to nine chlorines attached. The term, congener, is used to refer to a single, structurally-unique constituent of the mixture. In other words, at least 200 individual toxaphene congeners ~~make up the original toxaphene pesticide mixture. Individual congeners are often given their~~ own names, such as Hx-Sed, Hp-Sed, p26, or p50.

Technical Toxaphene Degrades in the Environment

In the OIG's review of the available scientific literature on the environmental degradation of technical toxaphene, we found numerous references to biotic and abiotic degradation, and to aerobic and anaerobic degradation. The aerobic degradation of technical toxaphene occurs at the slowest rate and has an aerobic half-life report of about 10-14 years (Fingerling, 1996). On the other hand, anaerobic degradation of technical toxaphene occurs at a much faster rate and has an anaerobic half-life of about 6 weeks. Therefore, since the use of toxaphene was severely restricted in 1982, any technical toxaphene left in the environment from 1982 or before has theoretically undergone two or more half-lives. Thus, at most, only 25 percent of the original starting material should theoretically still be present. By contrast, the only reported condition under which toxaphene does not degrade is autoclaved soil (i.e., all microbes in the soil have been killed off) (Fingerling 1996). Therefore, technical toxaphene is expected to degrade in the environment and its degradation is mediated primarily by microbes living in the soil.

Anticipated Toxaphene Degradation Products

Upon instrumental analysis by a gas chromatograph with electron capture detector (GC/ECD), the original technical mixture – a mixture of 200 or more congeners – produces a complex, multi-peaked chromatogram (see Figure 1B below). However, technical toxaphene is known to undergo microbial degradation in soil. Since the soil at the Hercules 009 Landfill site has been stabilized with cement, the free exchange of oxygen into the soil from the air is unlikely. Therefore, anaerobic microbial degradation is the most likely degradation process for the buried toxaphene waste at the Hercules 009 Landfill site.


(A) Toxaphene Degradation Products in Soil

(B) Technical Toxaphene

Figure 1: Chromatograms of Technical Toxaphene and Degraded Toxaphene are Completely Different

The major anaerobic microbial degradation products in soils or sediments are known to be Hx-Sed and Hp-Sed (Braekevelt, 2001). This microbial degradation of technical toxaphene produces a much simplified chromatogram (see Figure 1A above). Therefore, upon analysis at an environmental laboratory, the degraded toxaphene chromatogram appears completely different from the technical toxaphene chromatogram.

Although Hx-Sed and Hp-Sed are the major anaerobic degradation products in soil, degraded toxaphene chromatogram (see Figure 1A) also shows a significant number of other, less abundant anaerobic microbial degradation products. These less abundant toxaphene congeners in soil have been identified and are known to include p26, p50, p40, p41, and p44 (Maruya, 2001a). As discussed in more detail later, these less abundant toxaphene degradation products constitute the majority of risk to human health because they are not effectively metabolized by the body, which causes them to bioaccumulate. Hx-Sed and Hp-Sed are readily metabolized by the body and excreted, so they should not constitute a major risk to human health. However, since Hx-Sed and Hp-Sed are the major anaerobic degradation products, they are easier to detect than the other less abundant toxaphene congeners and could be used to indicate that toxaphene degradation products are present in the sample.

The implication of toxaphene's degradation is that humans are exposed to toxaphene's degradation products and not to the original technical toxaphene mixture (de Geus, 1999), (McHugh, 2003). Consequently, EPA's approach of using GC/ECD to test for the original technical toxaphene in the environment to identify toxaphene contamination is incorrect. EPA needs to test for individual toxaphene degradation products (i.e., specific congeners) in order to identify the presence or absence of toxaphene contamination in the environment.

Evaluating the Potential Risk to Humans from Toxaphene Exposure

Conducting a detailed and comprehensive risk assessment for the potential exposure to toxaphene from the Hercules 009 Landfill site is a complex task that is beyond the scope of this OIG review. Furthermore, detailed information is lacking on the potential human exposure to toxaphene degradation products and their toxicity, which limits the ability to conduct a thorough risk assessment. However, the potential risk to human health from toxaphene exposure can still be conceptually understood.

In general, a major factor needed to evaluate the level of risk to human health is to determine the ~~major human exposure pathways (sources) to toxaphene's degradation products and to determine~~ all potential sources. The Hercules 009 Landfill site is just one of the potential exposure sources. A toxaphene exposure study from the Netherlands used a model to estimate the exposure of the Dutch population to toxaphene (Fiolet and van Veen, 2001). This model identified that the main route of exposure to relatively soluble toxaphene congeners is approximately 80 percent from fish and 11 percent from drinking water. Another toxaphene exposure study, by Buranatrevedh, also concluded that the main route of exposure is about 93 percent from fish and about 7 percent from surface waters (Buranatrevedh, 2004). The remaining exposure routes (i.e., air and soil) are practically negligible. Based on these national toxaphene exposure studies, the main exposure risk to toxaphene is clearly from fish and from potential sources of drinking water. Although specific site conditions and other site specific variables at Hercules 009 Landfill will shift the relative levels for these various exposure routes, these national toxaphene exposure studies identify that the principal exposure routes of concern to the surrounding community are the fish in the diet and the potential for contaminated drinking water.

Another major factor needed to evaluate the level of risk to human health is what specific toxaphene congeners pose chronic risk to humans. The major toxaphene congeners found in fish are p26, p50, and p62; but p40, p41, and p44 are also present to a lesser extent (Fiolet and van Veen, 2001). The major anaerobic microbial degradation products in soils that may contaminate the groundwater are Hx-Sed and Hp-Sed, but p26, p50, p40, p41, and p44 are also found in soil to a lesser extent (Maruya, 2001a).

Although humans are exposed to a variety of toxaphene degradation congeners, most of these congeners can be rapidly metabolized via dechlorination, dehydrodechlorination, and oxidation, primarily through the action of the mixed function oxidase system and other hepatic microsomal enzymes (EPA Office of Water, 1999). For example, the primary toxaphene degradation products in soil (i.e., Hx-Sed and Hp-Sed) are expected to be easily metabolized and excreted with reported half-lives in fish of 5 and 13 days respectively (Smalling, 2004).

However, a limited number of toxaphene congeners (i.e., p26, p50, p40, p41) are poorly metabolized and can not be readily excreted, causing these congeners to accumulate in the body. These poorly metabolized congeners share a common structural pattern of alternating single chlorine substitutions (i.e., endo, exo) on the #2, #3, #5, and #6 carbons of the six-member ring (Maruya, 2000). Specifically, the poorly metabolized p26 and p50 congeners have half-lives of about 1 year in wild fish (Smalling, 2004). However, five toxaphene congeners (i.e., p26, p50, p40, p41, and p44) are not readily metabolized and excreted and, thus, can accumulate in the human body.

In order to evaluate the level of risk to human health, EPA needs to know the concentration of these five congeners and their metabolite precursors in the environment. Since these five toxaphene congeners represent the long-term chronic toxaphene exposure problem for humans, the toxicity of these five individual congeners, a mixture of these five congeners, or both, needs to be determined in more detail than is available in the scientific literature.

Human Exposure to Toxaphene Degradation Congeners

The following two academic studies have independently identified and documented human exposure to the individual toxaphene degradation congeners:

- In 1996, Dr. Gill used gas chromatography with negative ion mass spectroscopy (NIMS) to detect and measure toxaphene congeners in human blood serum (Gill, et al., 1997). Specifically, Dr. Gill's study documented the presence of p26, p50, p44, p40, and p41 congeners at a concentration of 2-200 parts per trillion (ppt) or up to 0.2 parts per billion (ppb) in human blood serum from Native Canadian communities. These five toxaphene congeners represented 95 percent of the toxaphene congeners found in human serum.

- In 2003, Dr. Barr used a sophisticated analytical technique to detect and measure toxaphene congeners in pooled human blood serum collected by the Red Cross in Atlanta in 1987, in Chicago in 1992, and in Cincinnati in 1994 (Barr, 2004). Specifically, Dr. Barr's study documented the presence of p26, p50, and possibly p40, p41, and p44 congeners at a concentration of 3-30 ppt (i.e., 0.03 ppb) in human blood serum from an undefined number of American blood donors.

These studies are critically important in identifying and simplifying the assessment of the risk to humans resulting from environmental exposure to toxaphene. These studies dramatically indicate that human risk is not to "technical" toxaphene's 200-plus congeners, but that the long-term chronic toxaphene exposure in humans is limited and simplified to just five toxaphene congeners (i.e., p26, p50, p40, p41, and p44) that the human body has difficulty metabolizing and eliminating, causing them to accumulate in the body.

Carcinogenicity of p26 and p50 Congeners

The EPA's Integrated Risk Information System (IRIS) database identifies technical toxaphene as a category B2 probable human carcinogen with a cancer potency factor of 1.1 mg/kg/day. However, there is limited scientific data on the carcinogenicity of persistent toxaphene degradation congeners, such as p26 and p50. But other chemical mixtures of congeners show that individual congeners can be significantly more carcinogenic than the original technical mixture. The classic example is dioxin, where 2,3,7,8-TCDD (tetrachlorodibenzo-*p*-dioxin) is up to 10,000 times more carcinogenic than other dioxin congeners. Another example is that bioaccumulated polychlorinated biphenyl (PCB) congeners appear to be more carcinogenic than the original "commercial" PCB mixture (EPA 7C-R293-NTSX). This clearly indicates that the carcinogenicity of the original technical toxaphene mixture cannot be applied to the carcinogenicity of the individual congeners, specifically, p26 and p50.

The European Union has conducted an Investigation into the Monitoring, Analysis, and Toxicity of Toxaphene in Marine Foodstuffs (MATT project). The MATT project predicted the tumor promoting potency of technical toxaphene and a cod liver extract (CLE) containing p26, p50, p62 in a bioassay measuring the inhibition of intracellular communication between Hepa1c1c7 cells (FAIR CT PL.96.3131). The CLE toxaphene congener mixture mimics the environmental exposure to the toxaphene congeners that are found in humans (e.g., p26, p50). The results reported from this bioassay indicate that the CLE toxaphene mixture is a more potent tumor promoter than the original technical toxaphene mixture. The MATT project estimated a tolerable daily intake ~~(TDI) to "weathered" toxaphene residues of 0.69 mg/kg/day. In general terms, the~~ MATT project's TDI estimate makes the toxaphene degradation products found in humans to be about twice as carcinogenic as the original technical toxaphene mixture. However, the report on the MATT project has not yet been peer reviewed.

An EPA Region 4 toxicologist believes that the conclusions reached in the MATT project may be incorrect and, in the response to the draft OIG report on the Hercules 009 Landfill, outlined why. Despite this, the MATT project is the sole toxicological study based on toxaphene degradation products and, thus, is chemically most relevant to human exposure. Region 4 may base its interim strategy for assessing the risk of toxaphene degradation products on the MATT laboratory study. The OIG believes more definitive toxicology studies are needed to verify the carcinogenicity of the individual p26 and p50 toxaphene congeners. Region 4 agreed that additional toxicity studies may be helpful and suggested additional research in the areas of in vitro testing of tumor promotion, whole animal developmental studies, and critical periods of exposure early or late in life.

Embryotoxicity of p26 and p50

In a 1997 study using a rat embryo culture model, the p26 and p50 toxaphene congeners caused abnormalities in the central nervous system (Calciu, 1997). The total morphological scores at 100 ng/ml for p26 and p50 were slightly worse than the total morphological score for the technical toxaphene. The significant finding from this study is that both the target site and type of toxicity are highly congener-specific. Therefore, the toxicity of technical toxaphene cannot and should not be used to predict the embryotoxic effects of the p26 and p50 congeners in humans. Thus, more scientific research is needed to evaluate the specific embryotoxic effects of p26 and p50 on humans.

Dr. Gill's study found concentrations of p26 and p50 at concentrations as high as 0.2 ppb in human blood serum (described above). The lowest dose in Dr. Calciu's rat embryo culture study was 100 ppb. The difference is a factor of 500, but the rat embryo culture study results represent only a 48-hour exposure to the rat embryos. This short exposure time does not directly correspond to human exposures to p26 and p50 over the full term of a pregnancy; human fetuses are exposed to a lower dose but for a longer period of time. Furthermore, the results from the rat embryo culture study represent dramatic development changes in which even subtle changes in human fetal development would be considered unacceptable. Therefore, additional research is needed to evaluate the potential for more subtle effects on embryo development when exposed to lower doses of p26 and p50 that correspond to actual human exposure levels. For example, in 1980, Dr. Olson observed behavior changes in rat offspring when pregnant rats were given low doses of technical toxaphene, p42a congener (referred to in the study as toxicant A), or p32 congener (referred to in the study as toxicant B) as measured by a swimming test and a maze retention test (Olson, 1980).

The embryotoxicity of toxaphene's persistent degradation products needs to be evaluated in the context of co-exposure with other persistent organochlorines (i.e., DDT/DDE, halogenated hydrocarbons (HCHs), and PCBs). The amount of p26 and p50 in human milk has been found to range from a low of 6 ug/kg lipid weight (i.e., ppb) in southern Canada to a high of 294 ug/kg lipid weight in Northern Quebec (Skopp, et al., 2002). This shows that babies are exposed through the mother's exposure to toxaphene degradation products before and after birth. Unfortunately, this observation about mother's milk is potentially problematic because an epidemiological study by Jacobson (Jacobson, 1996) indicates that developing embryos are the most susceptible target of organochlorines. Jacobson's study linked organochlorine exposure during fetal development to impaired cognitive development (e.g., low IQ scores).

Monitoring Should Identify Toxic Degradation Products

Monitored natural attenuation (MNA) is part of the remedy at Hercules 009 Landfill site. Superfund's MNA guidance (OSWER Directive 9200.4-17P) states EPA should evaluate for the potential presence of toxic transformation products. Toxaphene degradation products are a sub-category of transformation products. Specifically, the MNA guidance states:

> *The potential for creation of toxic transformation products is more likely to occur at non-petroleum release sites ... and should be evaluated to determine if implementation of a MNA remedy is appropriate and protective in the long term.*

Furthermore, the MNA guidance states:

> *... all [MNA] monitoring programs should be designed to accomplish the following: ... Identify any potentially toxic and/or mobile transformation products.*

Therefore, the Superfund's MNA guidance expects EPA to anticipate and to test for the presence of potentially toxic degradation products at hazardous waste sites. Since toxaphene is known to degrade in the environment and these degradation products are thought to be toxic, at Superfund sites suspected to contain toxaphene, EPA should evaluate the environmental samples for toxaphene's degradation products, specifically, the Hx-Sed and Hp-Sed congeners, but also the p26, p50, p40, p41, and p44 congeners.

EPA Method 8081 Tests for Technical Toxaphene

EPA Method 8081 is an analytical testing technique that uses GC/ECD. When an environmental sample is tested by the GC/ECD, the instrument produces a chromatogram as a record of what was contained in the sample (see Figure 2A).

Each peak in the chromatogram of a known technical toxaphene standard (see Figure 2B) represents 1 of the 200 unique congeners in the technical toxaphene mixture. There are actually so many peaks that they clump together in some areas of the chromatogram. Method 8081 detects toxaphene by identifying five peaks to the right of the red line in the environmental sample (see Figure 2A) and comparing their shape and position to five peaks to the right of the red line in a known technical toxaphene standard (see Figure 2B). In this example, since both chromatograms match on the right hand side, the laboratory would report that toxaphene is ~~present in this hypothetical environmental sample. EPA Method 8081 was designed and quite~~ dependable for detecting the original technical toxaphene mixture in an environmental sample.

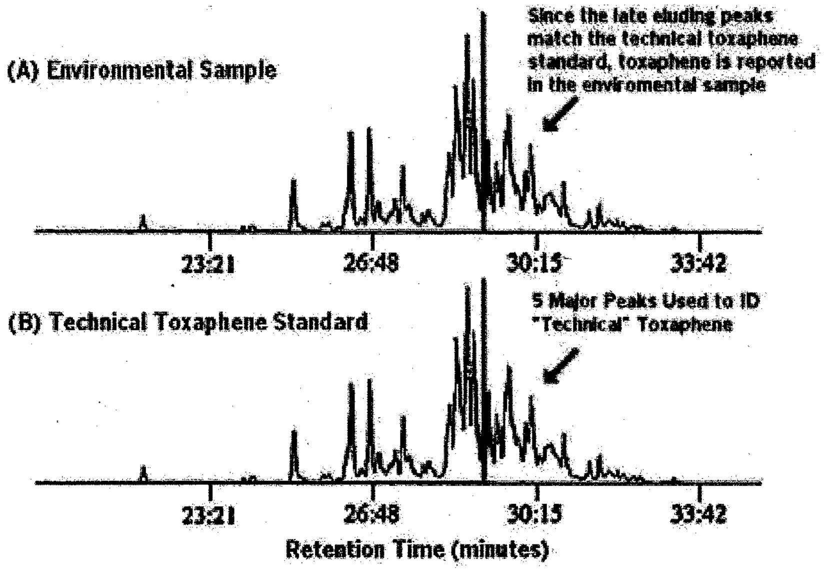
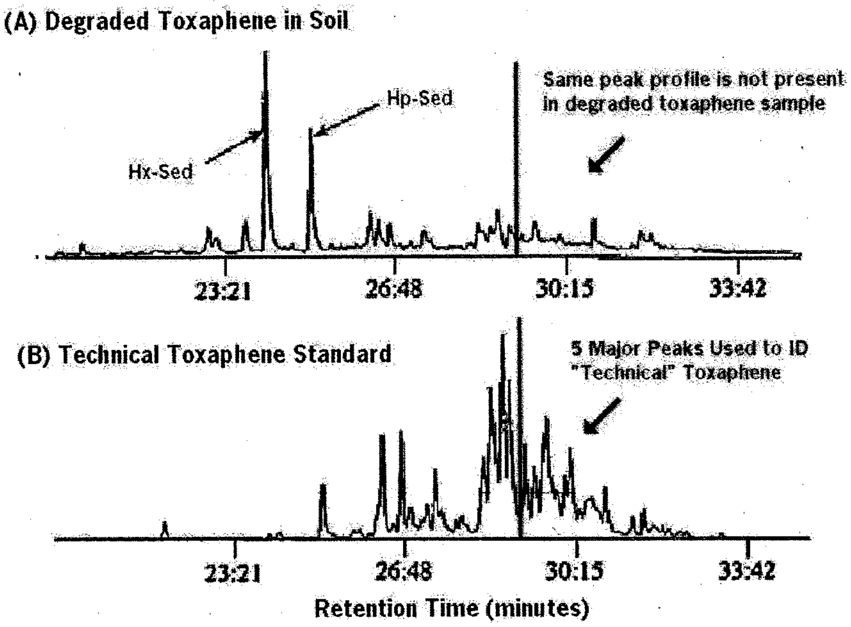


Figure 2: GC/ECD Chromatograms of Technical Toxaphene

EPA Method 8081 Does Not Identify Toxaphene Degradation Products

EPA Method 8081, which is listed in EPA's Test Methods for Evaluating Solid Waste, Physical/Chemical Methods (SW-846), uses a GC/ECD to analyze for the presence of toxaphene contamination. In order to identify the presence of a pollutant in an environmental sample, the retention time of a peak (representing a compound) in the sample's chromatogram is compared against the retention time of a known chemical standard. For the purposes of detecting toxaphene in a sample, EPA Method 8081 calls for a peak profile match against at least five peaks in the latter section of the toxaphene window (see the peaks after about 29 minutes in chromatogram 3B). In other words, the observed relative abundance of late eluting toxaphene congeners (i.e., octa- and nonachlorobornanes) has to closely match the relative abundance of the octa- and nonachlorobornane congeners found in the technical toxaphene standard. While EPA Method 8081 is appropriate and highly accurate for detecting technical toxaphene, it is not effective for detecting degraded toxaphene (i.e., "weathered" toxaphene) in environmental samples (e.g., soil, water, fish).

For demonstration purposes, chromatogram 3A below is a known chromatogram of toxaphene degradation products in soils. When chromatogram 3A is compared by EPA Method 8081's identification criteria for technical toxaphene, chromatogram 3A obviously does not have the same late eluding peak profile (i.e., the peaks after 29 minutes) as the technical toxaphene standard. Therefore, a match is not made and the presence of toxaphene is not reported by the laboratory, even though specific toxaphene congeners (e.g., Hx-Sed, Hp-Sed) are known to be present. This example demonstrates the manner in which EPA Method 8081 fails to detect toxaphene degradation products (i.e.,"weathered" toxaphene or individual toxaphene congeners) in environmental samples.


(A) Degraded Toxaphene in Soil

Same peak profile is not present in degraded toxaphene sample

(B) Technical Toxaphene Standard

5 Major Peaks Used to ID "Technical" Toxaphene

Figure 3: EPA Method 8081 Analyzes for Only Technical Toxaphene

An example of EPA Method 8081's failure to detect toxaphene's degradation products occurred in 1997 during the Georgia Department of Natural Resources' (GA/DNR's) study to measure the toxaphene levels in several species of fish and shellfish in and around Terry Creek. Terry Creek is another Superfund site in the Brunswick, Georgia, area that is contaminated with toxaphene due to previous manufacturing operations by Hercules Incorporated. The results of GA/DNR's study indicated no detectable quantities of toxaphene in every single fish sample analyzed. However, in 2001, Dr. Maruya of the Skidaway Institute of Oceanography re-analyzed the same fish and shellfish samples that were collected and analyzed by GA/DNR, but this time used both the GC/ECD technique and the NIMS congener-specific technique (Maruya, 2001b). The NIMS analytical technique was able to identify, while the GC/ECD technique was able to quantify, individual toxaphene congeners that were present in the fish samples at concentrations up to 1,420 parts per billion (ppb). The NIMS' identification of toxaphene contamination at Terry

Creek is in stark contrast to the results obtained by EPA Method 8081 alone that indicated no toxaphene contamination. Therefore, this example clearly shows that the analytical procedures specified in EPA Method 8081 do not identify degraded toxaphene in the environment.

Gas Chromatograph/Negative Ion Mass Spectrometry Can Be Used to Identify Toxaphene Degradation Products

Unlike the GC/ECD technique used in EPA Method 8081, NIMS can definitively and directly identify and measure individual toxaphene degradation products in the environment. The weakness in the GC/ECD technique used in EPA Method 8081 is that peak identification is based on only one factor: retention time. Therefore, even if the retention times match between the sample peak and the standard, the identity of the peak is still uncertain. By contrast, the NIMS technique uses two factors to identify peaks: retention time and a mass spectrum. A mass spectrum is analogous to a "fingerprint" of the compound. If the mass spectrum from the sample matches the mass spectrum of the standard, this definitively identifies the compound.

The NIMS methodology has been routinely used in academia since about 1993. For the last 5 years, the European MATT project has been using the NIMS method to monitor and document the levels of toxaphene degradation products in fish from the North Atlantic. Since the NIMS method has been developed and successfully implemented by others, EPA's formal validation and standardization of the NIMS method should not present any major technical difficulties. Also, including the NIMS method in SW-846 would significantly facilitate (1) the evaluation of toxaphene degradation products in the environment by the regulated community and (2) the gathering of congener-specific data needed for accurate risk assessments of exposure to toxaphene's degradation products.

Estimated Retention Time of Toxaphene Degradation Products

As described, EPA Method 8081 fails to identify toxaphene degradation products mainly because the identification criteria are based on seeing the late eluting peaks in technical toxaphene. However, an experienced chemist can still look for potential toxaphene degradation products in the GC/ECD data from the Hercules 009 Landfill. Although the Hercules 009 GC/ECD data do not include standards for the Hx-Sed and Hp-Sed toxaphene degradates, the expected retention time for Hx-Sed and Hp-Sed can be estimated from data published in the scientific literature (Figure 4 below). Since each technical toxaphene varies slightly by manufacturer, the technical toxaphene standard below is specifically from Hercules Incorporated in order to allow a subsequent comparison with the Hercules 009 Superfund site data. The estimated retention time window for the Hx-Sed and Hp-Sed toxaphene congeners, which are the main toxaphene congeners expected in anaerobic soil, occurs at the front edge of the technical toxaphene window. Notice that the Hx-Sed peak is to the left and taller than the Hp-Sed peak.

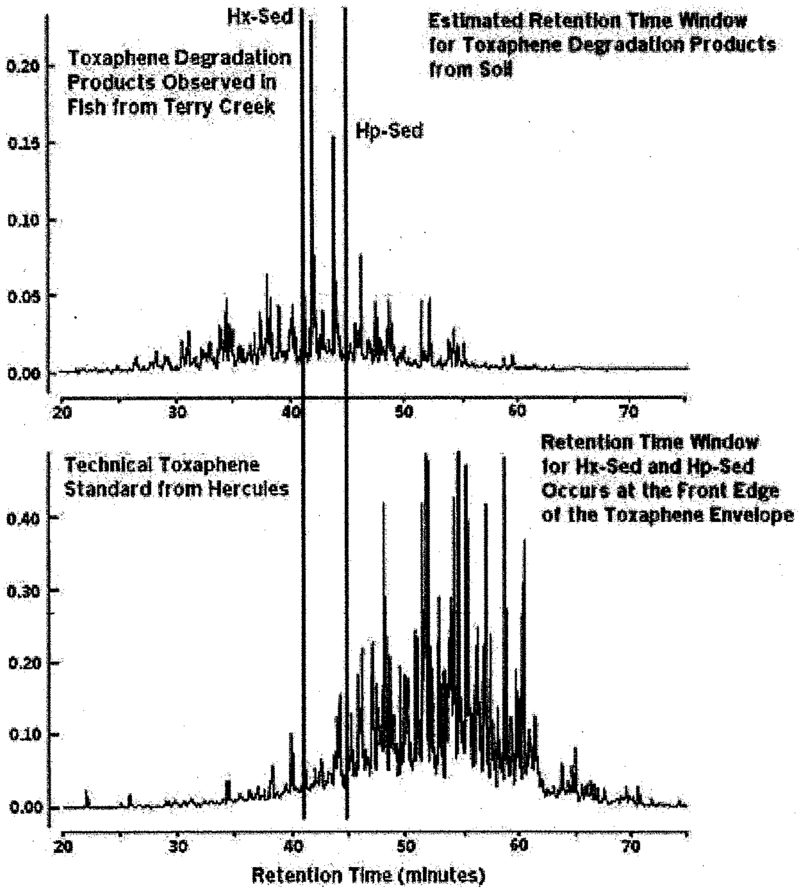
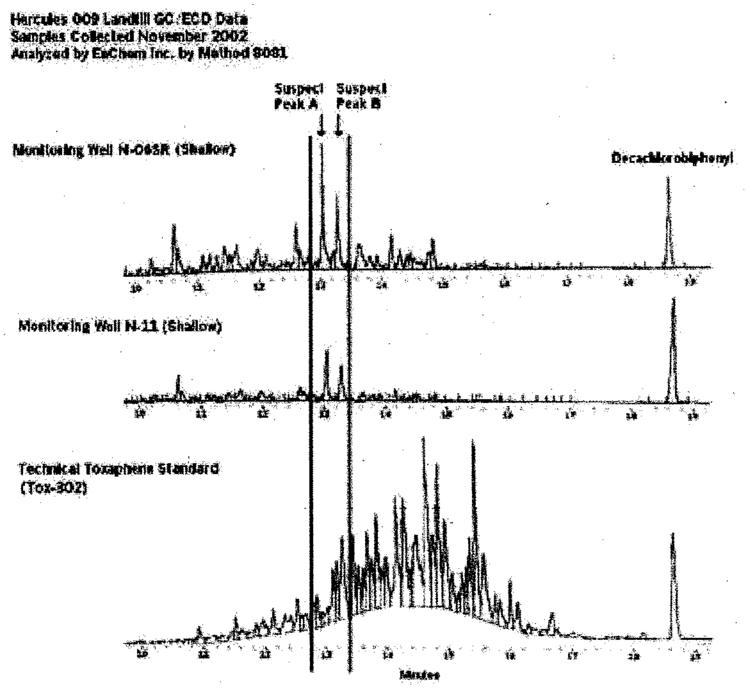


Figure 4: Estimated Retention Time Window for Hx-sed and Hp-sed

Hercules 009 GC/ECD Data Suggest Toxaphene Degradation Products May Be in the Groundwater

On January 8, 2003, the contractor for Hercules Incorporated, RMT Incorporated, provided EPA with the November 2002 groundwater sampling results, which were used in EPA's Hercules 009 Landfill 5-year review. RMT's subcontract laboratory (EnChem, Inc.) used EPA Method 8081A to analyze the toxaphene groundwater samples and reported nondetect (i.e., <5.2 micrograms per liter (ug/L)) for all toxaphene results. Fortunately, the sampling results included a chromatogram for each of the groundwater monitoring wells. This allowed for the comparison of the Hercules 009 Landfill groundwater samples against the Hercules technical toxaphene standard to check for the possibility of toxaphene degradation products (Figure 5 below).



Note: Chromatograms are normalized to the surrogate compound (Decachlorobiphenyl)

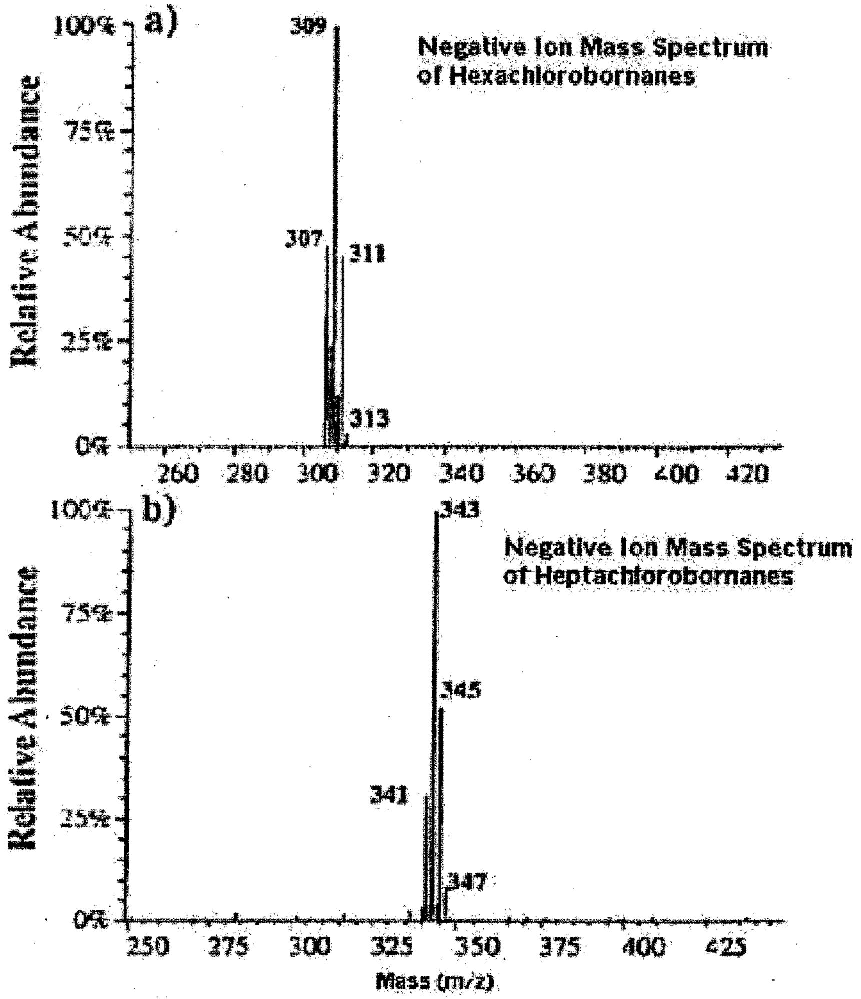
Figure 5: Potential Toxaphene Degradation Products in the Groundwater at Hercules 009 Landfill

As described in the previous section, the estimated retention time window for the Hx-Sed and Hp-Sed toxaphene congeners occurs at the front edge of the technical toxaphene window. When the estimated retention time window for Hx-Sed and Hp-Sed is superimposed on the chromatograms from monitoring wells N-06SR and N-11, two prominent peaks are present that resemble the Hx-Sed and Hp-Sed peak profile (i.e., the left peak is taller than the right peak). These chromatograms provide suggestive evidence that Hx-Sed and Hp-Sed might be present in the Hercules 009 Landfill groundwater. However, these peaks cannot be positively identified as toxaphene degradation products due to significant limitations in the data set. First, there are no Hx-Sed or Hp-Sed standards to establish their retention time, which is the key criterion for identifying compounds in a GC/ECD analysis (i.e., no standards; no identifications). Second, the critical weakness with all GC/ECD data is the lack of a mass spectrum that could be used to determine the structure of the compound making each of these peaks. The limitations of this GC/ECD data set clearly show the value of NIMS analysis.

If the samples had been run by NIMS instead of GC/ECD, a quick review of the mass spectra for each of the peaks could easily determine if these peaks were toxaphene congeners. For example, the negative ion mass spectrum for Suspect Peak A could be compared against the negative ion mass spectrum of hexachlorobornanes (Figure 6(a)). Likewise, the negative ion mass spectrum for Suspect Peak B could be compared against the negative ion mass spectrum of heptachlorobornanes (Figure 6(b)). If the spectra matched, EPA could conclude that there were toxaphene degradation products in the groundwater. However, with only the GC/ECD data, a definitive determination on the identity of these suspect peaks cannot be made.

NIMS Can Definitively Determine the Identity of Suspected Hx-Sed and Hp-Sed Peaks

NIMS could be used to definitively determine the identity of the Suspect A & B peaks observed in the Hercules 009 Landfill GC/ECD data (see Figure 5). The retention time and mass spectrum for Suspect Peak A would be compared against the retention time and mass spectrum for Hx-Sed. The mass spectrum for Hx-Sed looks like the diagram in Figure 6(a). The retention time and mass spectrum for Suspect Peak B would be compared against the retention time and mass spectrum for Hp-Sed. The mass spectrum for Hp-Sed looks like the diagram in Figure 6(b). The additional feature of the NIMS technique of comparing and matching a peak's mass spectrum allows for the definitive identification of the peaks.



Negative Ion Mass Spectrum of Hexachlorobornanes

Negative Ion Mass Spectrum of Heptachlorobornanes

Figure 6: Negative Ion Mass Spectrums for Hexachlorobornane and Heptachlorobornane

Testing for Toxaphene Degradation Products in Our Nation's Drinking Water Supply

Since the 1991 promulgation of the National Primary Drinking Water Regulations (NPDWR) for the Phase II Synthetic Organic Compounds, EPA has required drinking water suppliers to test for toxaphene in the Nation's drinking water supply. The 1991 NPDWR for toxaphene approved the use of EPA Methods 505, 508, and 525.1. However, EPA's Performance Evaluation studies show laboratories most frequently use EPA Method 508 to determine toxaphene concentrations in drinking water (EPA, 2003a). As part of EPA's Six Year Review of NPDWR that was completed on July 18, 2003 (68 FR 42907), EPA collected occurrence data on toxaphene in the drinking water supplies from a representative cross-section of 16 States. These occurrence data represent over 52,000 analytical results, mostly from 1994 to 1997 for approximately 14,000 public water systems (PWSs) (EPA, 2002). EPA's analysis identified only 6 detections of toxaphene in 41,516 ground water samples and only 7 detections of toxaphene in 10,913 surface water samples (EPA, 2003b, Table B.53.b). EPA concluded that no PWSs are expected to exceed EPA's Maximum Contaminant Level (MCL) of 3 ug/L for toxaphene.

Unfortunately, EPA Method 508 shares the same problem described above for EPA Method 8081 used in EPA's hazardous waste program. EPA Method 508 uses the same GC/ECD analytical instrumentation and, likewise, only identifies technical toxaphene through pattern recognition against a technical grade toxaphene standard. EPA Method 508 does not detect or report the potential presence of toxaphene degradation products in the water sample. Therefore, EPA's toxaphene occurrence data from PWSs should only be interpreted to mean that no technical toxaphene is expected to be found exceeding EPA's MCL of 3.0 ug/L.

EPA's toxaphene occurrence data from PWSs do not address the possible contamination of the ~~PWSs by toxaphene's degradation products. Volder and Li estimate at least 1.3 million tons of~~ toxaphene were released into the total global environment from 1950 to 1993 (Volder, 1993). In the United States, toxaphene has been weathering from at least 1982 when most agricultural uses were stopped by the EPA. Decades of microbial degradation of this technical toxaphene should have converted the majority of the original technical toxaphene mixture into a mixture of its degradation products. Therefore, any current potential toxaphene contamination of the Nation's drinking water supplies is not from the original technical toxaphene mixture, but from toxaphene's degradation products. Since toxaphene degradation products have a lower level of chlorination than technical toxaphene, the degradation products should be more water soluble and, thus, potentially more mobile than the original technical toxaphene. Thus, EPA needs to definitively evaluate the possibility that the Nation's ground water and/or surface drinking water supplies could have become contaminated by toxaphene's degradation products. Such an evaluation would require testing at representative PWSs with an EPA-approved congener-specific NIMS method.

Need Congener-Specific Testing and Congener-Specific Health Risk Information to Implement Accurate Fish Advisories

As previously identified, the major route of human exposure to toxaphene degradation products is through consuming contaminated fish. Therefore, the need to issue accurate and timely fish advisories is critical to protecting human health.

EPA's fact sheet on toxaphene fish advisories (EPA, 1999) states that toxaphene analysis, similar to PCB analysis, can be conducted to identify the presence of individual or specific congeners. However, the fact sheet also states that there are no standardized congener-specific methods or EPA-approved congener-specific methods for toxaphene at this time. Therefore, EPA recommends the analysis of total toxaphene until further development of congener-specific analyses. However, the lesson learned from the 1997 GA/DNR study at Terry Creek was that total toxaphene analyses can completely fail to detect degraded toxaphene in fish. A subsequent congener-specific NIMS analytical technique performed by Skidaway Institute of Oceanography was able to definitively identify and quantify individual toxaphene congeners present in the same Terry Creek fish extracts at concentrations up to 1,420 ppb. This event clearly shows the need for implementing an EPA-approved congener-specific toxaphene analysis to identify toxaphene contamination and to support subsequent health risk decisions such as fish advisories.

EPA's fact sheet on toxaphene fish advisories (EPA, 1999) also recommends fish consumption limits based on EPA's default risk assessment parameters for technical toxaphene. The reference dose (RfD) for technical toxaphene is used to calculate the noncancer health endpoint, while the cancer slope factor for technical toxaphene is used to calculate the cancer health endpoint. Unfortunately, using the toxicity of technical toxaphene is not an appropriate basis for two reasons. First, humans are only exposed to a subset of toxaphene congeners (i.e., the degradation products found in fish which are dominated by p26 and p50) and not to the full distribution of toxaphene congeners found in technical toxaphene. Second, the toxicity of each individual toxaphene congener can be expected to vary significantly from the toxicity observed from the exposure to the original technical toxaphene mixture. Therefore, EPA's use of technical toxaphene's RfD and cancer slope factor to quantify the risk from toxaphene degradation products in fish should at best be considered only an estimation. Thus, EPA needs to determine the toxicity of the persistent toxaphene degradation products found in fish (e.g., p26, p50) in order to accurately determine the potential risk to human health.

Technical Summary of Toxaphene Issue

EPA should recognize that toxaphene degrades in the environment and that all of EPA's toxaphene data collected using EPA Methods 8081 and 508 are inadequate to screen for toxaphene's degradation products. To address this problem, EPA should test toxaphene contamination using a congener-specific analytical method such as NIMS. EPA's validation and standardization of the NIMS method would facilitate evaluating toxaphene degradation products in the environment. EPA should recognize that the chronic health risk to humans is from the five persistent toxaphene congeners (i.e., p26, p50, p40, p41, and p44) that accumulate in the human body. EPA needs additional studies on the carcinogenicity and embryotoxicity of these five persistent toxaphene congeners to accurately evaluate the risk they pose to humans. Without congener-specific laboratory results and without knowing the toxicity of specific congeners, EPA is unable to definitively quantify the risk to human health posed by the toxaphene degradation products left in the environment and the food chain.

OIG Technical Conclusions

- The original "technical" toxaphene mixture degrades in the environment.

- The chronic health risk to humans is from exposure to toxaphene's persistent degradation products (e.g., p26, p50, p40, p41, p44) and not the original technical toxaphene mixture.

- EPA needs to use a congener-specific analytical method to positively identify and quantify toxaphene degradation products in the environment. The OIG recommends standardizing and validating the NIMS method and inserting an approved EPA NIMS method into SW-846 and the water program's testing methods.

- EPA needs to conduct specific research into both the carcinogenicity and embryotoxicity of the five persistent human toxaphene congeners (i.e., p26, p50, p40, p41, and p44) in order to develop acceptable human exposure limits to the individual congeners and/or to the mixture of these five congeners.

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Appendix B

Superfund Sites Listing Toxaphene as a Contaminant of Concern

EPA Identifier	Site Name	City	State
ALD007454085	T.H. Agriculture & Nutrition Co. (Montgomery Plant)	Montgomery	AL
CA5570024575	Travis Air Force Base	Travis AFB	CA
COD980499248	Lowry Landfill	Aurora	CO
COD980717953	Sand Creek Industrial	Commerce City	CO
FLD004092532	Stauffer Chemical Co (Tampa)	Tampa	FL
FLD053502696	Helena Chemical Co. (Tampa Plant)	Tampa	FL
FLD981021470	Wingate Road Municipal Incinerator Dump	Fort Lauderdale	FL
GAD003269578	Woolfolk Chemical Works, Inc.	Fort Valley	GA
GAD042101261	T.H. Agriculture & Nutrition Co. (Albany Plant)	Albany	GA
GAD980556906	Hercules 009 Landfill	Brunswick	GA
GAD991275686	Marzone Inc./Chevron Chemical Co.	Tifton	GA
NCD980843346	Aberdeen Pesticide Dumps	Aberdeen	NC
NCD981475932	FCX, Inc. (Washington Plant)	Washington	NC
NCD981927502	Geigy Chemical Corp. (Aberdeen Plant)	Aberdeen	NC
NJD064263817	Syncon Resins	South Kearny	NJ
SCD058753971	Helena Chemical Co. Landfill	Fairfax	SC

Appendix C

Agency Response to the Draft Report

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 26 2005

OFFICE OF THE
ADMINISTRATOR

MEMORANDUM

SUBJECT: EPA Response to OIG Draft Ombudsman Report, "More Information Is Needed On Toxaphene Degradation Products," Assignment 2004-1124

FROM: Marcus Peacock
Deputy Administrator

TO: Nikki L. Tinsley
Inspector General

Purpose

The purpose of this memorandum is to provide EPA comments on the Office of Inspector General (OIG) Draft Ombudsman Report, "More Information Is Needed On Toxaphene Degradation Products," Assignment 2004-1124.

Background/Discussion

The OIG has requested several EPA offices (OW, OSWER, OPPTS and ORD) to review the draft report dated August 12, 2005 entitled, "More Information Is Needed On Toxaphene Degradation Products: (OIG Assignment 2004-1124). The report describes the limitations of some EPA analytical methods for determining the insecticide toxaphene, and the lack of information on potential adverse health effects of toxaphene. EPA is urged to develop more sensitive and selective methods, and conduct more studies on the health effects of certain toxaphene degradates.

The various EPA Offices appreciated the opportunity to respond to this draft report. In general, EPA concurs with the recommendations. Attached are detailed comments from OSWER, OW and ORD. OPPTS was consulted and did not submit any comments. If your staff has any additional questions, please have them contact the following Special Assistants in the Office of the Administrator, Doreen Vetter at 564-1509 or Sarita Hoyt at 564-1471.

Attachment

cc: William Farland
Tom Dunne
Ben Grumbles
Susan Hazen
Dianne Bazzle
Patrice Kortuem

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EPA Comments on OIG Draft Ombudsman Report
More Information Is Needed on Toxaphene Degradation Products
Assignment 2004-1124

OFFICE OF RESEARCH AND DEVELOPMENT

1. On page 7, paragraph 3, the draft report states:

> 2. We recommend that the Administrator direct the Assistant Administrators for Research and Development, for Water, and for Solid Waste and Emergency Response to arrange for specific research into the dangers of tumors (i.e., cancer) and of harm to embryos posed principally by toxaphene degradation products p26, and p50, and perhaps by p40, p41, p44, and p62.

RESPONSE: We request the following change to this portion of the draft report:

> 2. We recommend that the Administrator direct the Assistant Administrators for Research and Development, for Water, and for Solid Waste and Emergency Response to arrange for specific research into the dangers of tumors (i.e., cancer) and of harm to embryos posed principally by a mixture of toxaphene congeners and metabolites found in fish.

Discussion: With respect to cancer and developmental effects, any future studies should focus on all congeners (Parlars 26, 40, 41 ,44, 50, 62) and the two congeners (Hx-Sed and Hp-Sed) that are originally present in technical toxaphene and increase greatly as a result of reductive dechlorination. Hence, any chronic bioassays that are designed for both cancer and developmental studies should include a mixture of all congeners that are present in fish and not individual congeners since humans will be consuming fish and not individual congeners.

2. On pages A-18 and A-19, we noted several issues with reference citations: AG

> Most references include author initials but a few (e.g., Braekevelt and Calciu) list the author's first name.
>
> References with multiple authors are cited in text as single authors (e.g., Maruya, 2001 or De Geus, 1999). They should be cited in text as "Maruya et al., 2001" or "De Geus et al., 1999."
>
> There are two Maruya et al., 2001 references but they are not differentiated with "a" and "b". There is no way for the reader to tell which reference is being cited.
>
> Fiolet and van Veen do not list any author initials at all. This reference is also misplaced alphabetically (should follow Fingerling et al.).
>
> Some journal titles are abbreviated but others aren't. The Smalling et al. citation doesn't include the journal title at all. Some cite "Vol." or "vol." and some just have the volume number alone. Some have "#" in front of the issue, others cite the issue number inside parentheses.

Most references capitalize all major words in the title but a few of them don't. Sometimes the year is cited before the volume/page numbers and sometimes after. The FAIR CT PL.96.3131 reference doesn't cite any year at all.

3. *Overview Comments*

Background: We have been involved in analytical methodology for about 30 years including most forms of chromatography, mass spectrometry, sample handling, and cleanup techniques. Two papers were published (see below: Brumley et al, 1993 and 1998) on the application of electron capture negative ion mass spectrometry (ECNIMS) including the toxaphene application as well as the related chlordane application. The negative ion approach has been around over 30 years and we have been involved in it since its very early stages.

Comments: The draft report presents certain recommendations concerning the analytical methodology used to determine toxaphene in real samples and other recommendations concerning toxicology of toxaphene. Our comments are restricted to the analytical chemistry aspects.

The analytical chemistry recommendations concern issues of toxaphene degradation and perceived deficiencies in the analytical methodology and a recommendation to change to the ECNIMS methodology as is currently performed throughout many parts of the world. ECNIMS has been in existence for decades and ORD has supported its inclusion in the tool kit of EPA chemists by generating the publications cited above. However, we have no official methods that use chemical ionization mass spectrometry at all, positive or negative ion. We have no GC/GC/MS or GC/MS/MS methodologies in place. We have no LC/MS methodology in place that uses ESI. Rather we have a methodology that uses Thermospray Ionization, a technique that few if any laboratories still retain in their instruments.

In the particular case of the toxaphene issue here, we support the recommendation to pursue modern methods involving ECNIMS. The complementary and screening use of GC/ECD is highly recommended along with the inclusion of the degradation products in the methodology. Cases of positive samples or indeterminate samples can be submitted for GC/ECNIMS as needed to support the findings. The basic finding of the draft report is that the science as currently practiced in this analysis is inadequate to do the task that needs to be done. We concur in this conclusion.

One issue concerns the availability of instrumentation to carry out ECNIMS. This capability is included in many instruments along with EI (Agilent instruments, for example) if the option is selected. One difficulty is that an ion source changeover is often required which is a day of down time because of equilibration and gas purging. This may be reduced on recent instruments capable of a more rapid switchover. It does imply that production laboratories would probably keep a dedicated instrument for this technique, depending on sample load. The technique is reliable, reproducible, quantitative, and practical so that misinformation that has been circulated in the past about ECNIMS should be disregarded. It is obvious that laboratories in the U.S. and throughout the world are able to perform this technique without difficulty.

Citations:

W. C. Brumley, C. M. Brownrigg, and A. H. Grange, "Determination of Toxaphene in Soil by Electron Capture Negative Ion Mass Spectrometry After Fractionation by High Performance Gel Permeation Chromatography," J. Chromatogr., 633, 177-183 (1993).

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OFFICE OF SOLID WASTE AND EMERGENCY RESPONSE

ASSESSMENT AND REMEDIATION DIVISION: OSRTI agrees with the conclusion that research is needed in reproductive, mutagenic, and carcinogenic toxicity of toxaphene degradation products. However, the decision to fund this specific research should be balanced against other research needs of the Superfund program.

OFFICE OF SUPERFUND REMEDIATION AND TECHNOLOGY INNOVATION
The IG report recommends that we validate and use a particular method for testing for toxaphene degradation products. It also recommends that EPA address risk assessment related issues.

Background: The Analytical Services Branch (ASB, within Superfund) typically does not consider the kinds of issues discussed in this report (science, policy and research questions that address risk and method validation). We generally do provide services to site managers that are well established and frequently requested. As a result, from an ASB perspective, these recommendations do not affect us directly. The current Contract Lab Program does not have the capability to run the recommended ~~analyses, nor do our non-routine analytical services contracts. However, should site managers care to~~ request these new analyses, we might assist in finding contract vehicles that could provide these services in a cost effective manner. At the current time, in order for Remedial Project Managers or On-Scene Coordinators to conduct these kinds of analyses (or other more innovative kinds of methods), they would need to establish task orders with labs using the RAC, START or other regional contract vehicles. As a result, ASB is neutral in our reaction to these recommendations.

Discussion: However, we do have the following additional thoughts (which are touched on in this report):

Before a site manager or OSC would order this kind of work, they would need confirmation that levels of these degradation products in the environment present health (or environmental) risks of concern to our Superfund communities. This would argue that the risk questions be addressed first. Addressing the risk (associated with levels in the environment) will in part then drive the requirements for the methods.

Secondly, while the proposed method may be a reasonable means to improve recognition of the specific degradation products, it is not clear from the report whether alternative approaches have also been evaluated. It may be more cost effective (for the cleanup industry, broadly speaking) for EPA to identify methods that can be run utilizing the kinds of equipment currently available at many commercial environmental labs.

OFFICE OF SOLID WASTE

General Comments:

- While OSW concurs with the OIG Ombudsman findings and recommendations, we have some issues and concerns regarding the presentation of technical discussions which result in some incorrect statements in the report, which we will clarify in the specific comments.

- Also there appear to be some technical contradictions in statements addressing the comparison of applicability between the GC/ECD methods and the NIMS method in the sections of Appendix A.

- With the promulgation of the Methods Innovation Rule on June 14, 2005 (70 FR 34537, June 14, 2005), OSW removed the final barriers to completely allowing the use of the performance-based measurement system (PBMS) for RCRA analyses. Under PBMS, any appropriate method may be used, whether it is published in SW-846 or is from an alternative source, provided that it can be demonstrated to generate data of known and appropriate quality that can be used for its intended application. Under the PBMS paradigm, a NIMS method that can be validated for a site-specific application may be used for analyzing toxaphene degradation products for RCRA applications.

- The problems encountered with the data generated from the GC/ECD methods, (e.g., Method 8081), are not because of the method's lack of capability, but of inappropriate application of the method in the project planning process. If toxaphene degradation products are not included or requested as target analytes in the planning documents, it does not matter whether you use GC/ECD or NIMS for the analysis. These analytes will not be reported in either case.

- An additional finding and recommendation should be that "Toxaphene degradation products should be included as target analytes for analyses at toxaphene-containing sites."

- OSW agrees that the NIMS methodology would make for easier definitive identification of toxaphene degradation products and any other organochlorine pesticides than would GC/ECD because of the enhanced analyte identification capabilities of the mass spectrometer.

Specific Comments:

- At a Glance, pg. 3 of 35: In the third sentence beginning with "The analytical methods...", "are not designed to identify" should be changed to "are not normally used to identify". If toxaphene degradation products were identified as target analytes and standards obtained for them during the project planning process, then the existing ECD methods could be used to identify these degradation products. However, the results will not be produced nor reported unless specific actions to include them in the analytical planning process are done.

- Section "A Different Analytical Method Is Needed...", pg. 5: In the first sentence, please change "...do not evaluate..." to "... are not normally used to evaluate..." Please add the following to the end of the second sentence: "...mixture, 'but have not been formally validated for toxaphene degradation products'".

- Please change the title of the Topic on pg. A-8 from "EPA Method 8081 Does Not Identify Toxaphene Degradation Products" to "EPA Method 8081 Is Not Normally Used to Identify Toxaphene Degradation Products". Figure 3A is an excellent GC/ECD chromatogram which shows clearly identified peaks for the toxaphene degradation products, Hx-Sed and Hp-Sed. Use of an appropriate standards chromatogram for comparison would result in valid qualitative and quantitiative identification of these compounds by GC/ECD, which directly contradicts the statements in this section to the contrary.

- The comparison discrepancies reported on pg. A-9 between the NIMS results and the Method 8081 results were not primarily due to differences in the analytical capabilities of the methods, but due to differences in reporting requirements with respect to which compounds were actually target analytes for the application of each method. The key advantage of the NIMS method over GC/ECD for single component or congener-specific analytes is the direct definitive identification that mass spectrometry provides. Use of a non-specific GC detector, such as ECD, requires an additional confirmation step to complete the compound identification.

- On pg. A-10, in the first sentence of the Section "Gas Chromatograph/Negative Ion Mass Spectrometry Can ...", please add the following wording, "...NIMS can definitively 'and directly' identify and measure..."

OFFICE OF WATER

Background

The Office of the Inspector General (OIG) has asked several EPA offices to review a draft report dated August 12, 2005 and titled More Information Is Needed On Toxaphene Degradation Products (OIG Assignment 2004-1124). The authors of this draft report describe limitations of some EPA analytical methods for determination of the insecticide toxaphene, and the lack of information on potential adverse health effects of toxaphene. The authors urge EPA to develop more sensitive and selective methods, and conduct more studies on the health effects of certain toxaphene degradates. The Office of Water, which has the responsibility for monitoring pollutants in water, is responding to the recommendations for development of better methods for toxaphene. We have identified two EPA analytical methods that can measure toxaphene degradates in water.

Discussion

Toxaphene is a complex mixture of over 200 very similar chlorinated compounds known as toxaphene congeners. Congeners differ in the number and location of chlorine atoms. In a water or soil environment the relative proportions of the individual chlorinated congeners change (i.e. weathers or degrades) as the original mixture loses chlorine. The authors note that some EPA methods do not measure seven specific toxaphene congeners that have been identified at a Superfund site in Georgia. They refer to these congeners as "degradation products", and recommend that EPA approve a method that uses a negative ion mass spectrometry (NIMS) technology to determine these products. We have evaluated this technology, and agree that it could provide another sensitive method for determination of individual toxaphene congeners. However, in addition to approved non-mass spectrometry (MS) methods EPA 508 and 608 that only determine toxaphene as mixtures of congeners, MS methods (EPA 525.2 and 1625) are capable of determining low levels of specific congeners.

Prof. Ronald Hites of Indiana University developed a NIMS method (Anly. Chem. 59, 913-917; 1987) for ORD that later was used in Region 5 to measure toxaphene degradation products in Great Lakes' sediment (J. Great Lakes 25(2): 383-394; 1999). This is the method which the authors of the OIG report attribute to a European source. Although this NIMS method will not provide a major increase in selectivity relative to the EPA MS methods, it may provide better sensitivity in "dirty" samples because interferences often do not easily ionize in the negative ion mode. The NIMS method is available for use and has been used in the Great Lakes Program though it has not yet been fully validated by EPA or published in the Federal Register.

Toxaphene is of environmental interest, but the use and production of toxaphene has been banned since 1990. Our present chemical method development efforts are fully focused on developing robust methods for determinations of complex classes of pollutants that are used in increasing amounts, and transported into our waterways. These pollutants include personal care products, pharmaceuticals, currently registered pesticides (and degradates), and other emerging pollutants. Although validation of additional methods for toxaphene is not an Office of Water priority, we are available for questions about application of the NIMS method, or our EPA MS methods to measurements of toxaphene congeners in the environment.

OIG Technical Comments on the Agency Response

OIG Draft Recommendation 1:

We recommend that the Administrator direct the Assistant Administrators for Water and for Solid Waste and Emergency Response to:

a. Develop, validate, and approve the gas chromatograph with negative ion mass spectroscopy method to analyze toxaphene degradation products, especially p26, p40, p41, p50, p62, Hx-Sed, and Hp-Sed, and

b. Use the new method to analyze environmental samples in their programs.

OIG Technical Comments on EPA's Response:

We agree with the comments provided by EPA's Office of Research and Development (ORD) concerning using the gas chromatograph/negative ion mass spectrometry (NIMS) method for detecting and documenting environmental contamination by toxaphene degradation products. Specifically, we want to highlight and comment on the following points in ORD's response:

- ORD states that EPA has no official NIMS method and supports including the NIMS method into EPA's "tool kit." We agree with ORD that the NIMS needs to be approved as an EPA method so that the method is readily available to EPA staff and the regulated community to evaluate and test for degraded toxaphene in the environment.

- ORD states that "... the science as currently practiced in the analysis [of toxaphene] is inadequate to do the task that needs to be done." This is consistent with our position that technical toxaphene degrades in the environment and the current use of EPA's GC/ECD method does not adequately detect potential human exposure to toxaphene's degradation products left in the environment.

- ORD states that "The [NIMS] technique is reliable, reproducible, quantitative, and practical..." We also found this to be true about the NIMS technique; no technical or practical issues prevent EPA programs from using NIMS.

We have the following comments regarding the response from the Office of Solid Waste and Emergency Response (OSWER):

- The Analytical Services Branch (ASB) within the Superfund program indicates that ASB has a "neutral" opinion on the development, validation, and approval of a NIMS method. ASB indicates it is up to the Remedial Project Manager (RPM) and On-Scene Coordinators (OSC) to conduct these "...more innovative kinds of methods." In our opinion, it is impractical to expect RPMs and OSCs to have the necessary laboratory skills, time, and resources to develop, validate, and implement the "innovative" NIMS on a site-specific basis. RPMs and OSCs will probably continue to choose an already approved EPA method (e.g., Method 8081) from EPA's pre-existing "tool kit" of analytical methods (even though it is not exactly what is needed), rather than validate a new NIMS method themselves.

- ASB's comments do not address the problem of evaluating for toxaphene degradation products at Superfund sites being addressed by potentially responsible parties (PRP), which are the majority of Superfund sites. PRPs are reluctant to use an unapproved EPA method, because EPA may not accept the validity of the data from the unapproved method. Analogous to RPMs and OSCs, PRPs would prefer to continue to choose an already approved EPA method (e.g., Method 8081) to evaluate for degraded toxaphene at a Superfund site rather than have to validate an unapproved NIMS method. Hence, we insist that EPA validate and approve the NIMS method to facilitate its use by RPMs, OSCs, and PRPs instead of each user having to separately validate the NIMS method each time it is used.

- ASB expresses concern that the analytical equipment at commercial analytical laboratories is not capable of running the NIMS method. To the contrary, we found that most commercially available gas chromatograph-mass spectrograph instruments (e.g., Agilent instruments – f.n.a. Hewlett-Packard) have the capability to run the NIMS method (i.e., a lab would need to purchase the chemical ionization option for the instrument). This equipment issue is directly addressed in ORD's comments. Due to configuration issues with the hardware of a gas chromatograph-mass spectrograph, we ~~agree with ORD's opinion that a commercial laboratory would probably have to dedicate~~ a single instrument for the NIMS analyses.

- The Office of Solid Waste (OSW) indicates that the analytical procedures specified in EPA Method 8081 were not designed or validated to analyze for toxaphene degradation products. However, OSW indicates that the GC/ECD analytical technique used in EPA Method 8081 could be developed to detect toxaphene degradation products (e.g., add individual toxaphene congeners as target compounds and use the appropriate toxaphene congeners as standards). We concur with OSW that EPA Method 8081 was never designed or validated to detect degraded toxaphene. Furthermore, we conceptually agree that the GC/ECD technique could be developed to detect toxaphene degradation products, but we do not advocate this course of action because the compound identification by the GC/ECD technique is inherently inferior to the compound identification by GC/NIMS due to the presence of a mass spectrum for identifying the peaks.

- OSW indicates the problems encountered with detecting toxaphene degradation products by EPA Method 8081 were due to inappropriately applying EPA Method 8081 during the project planning process. We agree that EPA Method 8081 should not be used to evaluate for degraded toxaphene products in the environment (i.e., EPA Method 8081 does not list individual toxaphene congeners as target compounds). However, we stress that EPA's project planning process at Superfund sites needs to recognize that technical toxaphene degrades in the environment and that NIMS is the best available method to detect and identify the extent of degraded toxaphene.

- OSW states that under the performance-based measurement system (PBMS) for RCRA analyses, any method (EPA approved or not) can be used "… provided that it can be demonstrated to generate data of known and appropriate quality …" Therefore, OSW defers to the site managers to validate the method for each site-specific application. As with the Superfund program, in our opinion, the expectation that site managers have the necessary laboratory skills, time, and resources to develop, validate, and implement the "innovative" NIMS on a site-specific basis is impractical. As a result, site managers will probably continue to choose an already approved EPA method (e.g., Method 8081) from EPA's pre-existing "tool kit" of analytical methods (even though it is not exactly what is needed), rather than validate a new NIMS method themselves.

- OSW suggests the following additional recommendation: "Toxaphene degradation products be included as target analytes for analyses at toxaphene-containing sites." We agree with this suggestion and have incorporated similar language into recommendation 1b.

- OSW states that "… the NIMS would make for easier definitive identification of toxaphene degradation products and any other organochlorine pesticides than would GC/ECD because of the enhanced analyte identification capabilities of the mass spectrometer." We agree with OSW that NIMS' superior identification capabilities are needed to clearly identify individual congeners from such a complex mixture of congeners and other non-toxaphene peaks found in environmental samples.

We had the following comments regarding the response from the Office of Water (OW):

- OW's response indicates that the NIMS method only provides another sensitive method for the determination of individual toxaphene congeners. Specifically, OW states that "… MS [mass spectrometry] methods (EPA 525.2 and 1625) are capable of determining low levels of specific congeners." We disagree with OW's assessment of the value and utility of the existing methods. EPA Methods 525.2 and 1625 use electron ionization mass spectrometry that is inherently less sensitive than existing methods that use gas chromatography with electron capture detectors, i.e., EPA Methods 508 and 608. The NIMS method is the only practical mass spectrometry method that has the same sensitivity as the GC/ECD methods. EPA method 525.2 lists only toxaphene (a.k.a., technical toxaphene) as a target compound. Also, EPA method 525.2 does not identify individual toxaphene congeners. Furthermore, EPA method 1625 does not even list toxaphene as a target compound for the analysis.

- OW's response does not address the continued testing of drinking water for toxaphene at public water systems, which mostly use EPA's GC/ECD Method 508. These resulting data can only be interpreted to mean that no technical toxaphene is in our Nation's drinking water. Since toxaphene has been banned since 1990 and is known to degrade in the environment, one would not expect to find technical toxaphene in our Nation's

> drinking water, but would expect to find environmentally degraded toxaphene in the water. Therefore, OW's 1991 National Primary Drinking Water Regulations requiring public water systems to continue testing for technical toxaphene wastes the time and resources of public water systems. OW needs to approve and use the NIMS method to evaluate our Nation's drinking water for possible contamination by degraded toxaphene.

In conclusion, after considering EPA's response, we are committed to having EPA approve and use the NIMS to evaluate for degraded toxaphene in the environment. Furthermore, based on EPA's response, we believe that recommendation 1b needs to be revised to require EPA to evaluate sites that are known to have contained technical toxaphene to be evaluated for the presence of toxaphene degradation products by the NIMS method.

OIG Draft Recommendation 2:

We recommend that the Administrator direct the Assistant Administrators for Research and Development, for Water, and for Solid Waste and Emergency Response to arrange for specific research into the dangers of tumors (i.e., cancer) and of harm to embryos posed principally by toxaphene degradation products p26, and p50, and perhaps by p40, p41, p44, and p62.

OIG Technical Comments on EPA's Response:

We agree with the comments provided by EPA's ORD concerning the research into the human toxicity of toxaphene degradation products. ORD requests revising the wording of the first recommendation from "...posed principally by toxaphene degradation products p26, and p50, and perhaps by p40, p41, p44, and p62" to "...posed by a mixture of toxaphene congeners and metabolites found in fish." We concur with this wording change. Since the vast majority of human exposure is through eating fish, the wording change allows ORD to assess the toxicity and characterize the risk from the degradation mixture to which humans are most exposed. Furthermore, the wording change still allows ORD to study the toxicity of the individual degradation congeners that are poorly metabolized and not readily excreted from the body (i.e., p26 and p50). In short, the wording change allows ORD more flexibility in studying the toxicity of toxaphene degradation products.

We disagree with the comments provided by OSWER's ASB that the health risks from toxaphene degradation products should be addressed before developing and implementing the NIMS method. Our opinion is that the NIMS methodology is already being successfully implemented by the European Union and would require only a minimum amount of effort and resources to be validated and approved by EPA. The immediate need for an EPA-approved NIMS method is clearly demonstrated by Skidaway Institute of Oceanography's successful use of the NIMS in 2001 to document high concentrations of toxaphene degradation congeners in fish near the Terry Creek Superfund site in Brunswick, GA. By contrast, the research needed to characterize the human health risks posed by toxaphene degradation products is anticipated to take about 6 years to complete.

EPA OW's response did not specifically address the need to research the human toxicity of toxaphene degradation products. OW's MCL for toxaphene in drinking water is 3.0 ug/L. This is the regulatory limit for the acceptable human exposure to technical toxaphene in drinking water. However, since toxaphene has been banned since 1990 and is known to degrade in the environment, human exposure in our Nation's drinking water would currently be to degraded toxaphene, and not to technical toxaphene. Therefore, in our opinion, due to the lack of potential exposure to technical toxaphene in our Nation's drinking water, the OW's MCL for technical toxaphene is outdated. However, since toxaphene was a heavily used pesticide in the United States, there is a potential human exposure to toxaphene degradation products in our Nation's drinking water. Therefore, OW should be interested in ORD's reseach into the toxicity of toxaphene degradation products because OW will need the research if it becomes necessary to establish a health effects limit for toxaphene degradation products in drinking water.

In conclusion, after considering EPA's response, we will incorporate ORD's revised wording into the second recommendation.

Distribution

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 3 0 2006

DEPUTY ADMINISTRATOR

MEMORANDUM

SUBJECT: Response to Ombudsman Report, *More Information is Needed on Toxaphene Degradation Products*, Report No. 2006-P-00007, dated December 16, 2005

FROM: Marcus Peacock MP

TO: ~~Bill A. Roderick~~ Bill
Acting Inspector General

This is in response to your memorandum dated July 14, 2006, requesting additional information on the U.S. Environmental Protection Agency's response to the subject report.

Your memorandum specifically requested a milestone date for completing the Office of Research and Development's (ORD) Multi-Year Research Plan (MYP) and the Office of Water's (OW) prioritization process. The ORD MYP for Land (which includes Superfund and Resource Conservation and Recovery Act) and Drinking Water will be finalized by December 30, 2006. The process by which OW identifies contaminants for methods development and regulation is an ongoing one, but the office expects to complete the third Contaminant Candidate List by August 2009.

We are pleased that the Office of the Inspector General (OIG) finds the Agency's actions already underway to be acceptable and responsive to the report's recommendations. We request the report be closed in the OIG tracking system so that we may track the corrective actions.

If you or your staff have additional questions, please have them contact the following Special Assistants in the Office of the Administrator: Doreen Vetter, at (202) 564-1509, or Laurie Dubriel, at (202) 564-4031.

cc: Benjamin Grumbles
Susan Bodine
George Gray

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 19 2006

OFFICE OF
INSPECTOR GENERAL

MEMORANDUM

SUBJECT: Ombudsman Report 2006-P-00007
More Information Is Needed on Toxaphene Degradation Products

FROM: Bill A. Roderick
Acting Inspector General

TO: Marcus Peacock
Deputy Administrator

Thank you for the milestone dates provided in your memorandum of August 30, 2006, for two of the actions planned in response to the subject report. These dates, together with the dates already identified in your memorandum of March 22, 2006, allow us to close this report in our tracking system. So the Management Audit Tracking System will allow the three Assistant Administrators to monitor the corrective actions for which they are responsible, we will add them as action officials as we close the report in our system. We look forward to EPA having the new analytical method available and seeing toxaphene degradation products in the Multi-Year Research Plan and Contaminant Candidate List.

If you or your staff have questions regarding this matter, please contact me at 202-566-0847 or Eileen McMahon, the Assistant Inspector General for Congressional and Public Liaison, at 202-566-2546.

cc: Benjamin Grumbles, Assistant Administrator for Water
Susan Bodine, Assistant Administrator for Solid Waste and Emergency Response
George Gray, Assistant Administrator for Research and Development
Laurie Dubriel, Special Assistant to the Administrator
Pat Gilchriest, OA Audit Liaison
Johnsie Webster, OSWER Audit Liaison
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Cheryl Varkalis, ORD Audit Liaison
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ATSDR | Department of Health and Human Services
Agency for Toxic Substances & Disease Registry

PUBLIC HEALTH ASSESSMENT

TERRY CREEK DREDGE SPOIL AREAS/HERCULES OUTFALL SITE
BRUNSWICK, GLYNN COUNTY, GEORGIA

SUMMARY

The Terry Creek Dredge Spoil Areas/Hercules Outfall site (the Terry Creek site) is in the city of Brunswick, Glynn County, Georgia. The site comprises two dredge spoil areas, a mobile home park, and the Hercules Outfall. It was proposed to USEPA's EXIT National Priorities List (NPL) on April 1, 1997. The two dredge spoil areas contain contaminated sediments dredged from the Dupree and Terry Creeks and placed in adjacent tidal marshes. The outfall area, where Hercules Inc.--a former pesticide plant--discharges waste water to Dupree Creek, as well as Terry and Dupree Creeks and adjacent surface water drainage areas, are part of the site. The Hercules, Inc. facility itself, however, is not part of this proposed NPL site. From 1948 through December 1980, Hercules (formerly known as Hercules Powder Company) produced as a major product toxaphene, a polychlorinated camphene (PCC) insecticide. Since 1972, when PCC in waste effluent from the Hercules manufacturing plant in Terry and Dupree Creeks was first restricted, the concentration of PCC in environmental samples such as sediment and fish has decreased significantly. In that regard, it is important to note that Terry and Dupree Creeks are used for fishing and crabbing.

Seafood consumption remains the main source of toxaphene exposure for people at and near the Terry Creek site. Components of technical grade toxaphene, its breakdown products or both have been detected in edible fish at Dupree and Terry Creeks. Thus additional, current information on quantitative and qualitative determinations of PCC residues in seafood from the Terry Creek area is needed. Such information will reduce any uncertainty regarding the level of toxaphene in fish, as well as the toxicologic meaning of such data. Accordingly, based on these data gaps, ATSDR considers this site to be an indeterminate public health hazard.

ATSDR recommends limiting consumption of contaminated seafood from Dupree and Terry Creeks. During the cleanup of PCC-contaminated sediments, the Georgia Environmental Protection Division, Coastal Resources Division, and the US Environmental Protection Agency recommend that people refrain from fishing or swimming in all of Dupree Creek and Terry Creek north of Torras Causeway to 2 mile west of its confluence with the Back River. Next spring, GA EPD will update the fish consumption guidance for this site, based on fish species at different locations. Moreover, because of contamination with PCBs and mercury from unknown sources, the GA DEP and USEPA recommend that consumption of silver perch (yellowtail) caught south of Torras Causeway to Lanier Basin be limited to one meal per week. According to the National Shellfish Sanitation Program standards--which are based on biological hazards--clams, mussels, and oysters in these waters are deemed not edible. Still, people eating fish from nearby areas can lower their risk of ingesting organic contaminants such as polychlorinated biphenyls (PCBs) by removing fatty tissue before cooking as well as by eating small (i.e., younger) fish.

Limited potential for human exposure exists at levels that would be of health concern in other exposure pathways such as soil, sediment, surface water or groundwater. Although unrelated to the Terry Creek site, based on community concerns and data collected by the Georgia Department of Natural Resources, ATSDR will continue to evaluate air data, if new data becomes available. Also, although asthma is a common health complaint of residents living near the site, the cause of that asthma is unknown.

BACKGROUND

In this public health assessment, the Agency for Toxic Substances and Disease Registry (ATSDR) evaluates the public health importance of the Terry Creek Dredge Spoil Areas/Hercules Outfall (the Terry Creek site) in Brunswick, Georgia. In April 1997 this site was proposed to the National Priorities List (NPL). The Superfund law (the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 [CERCLA] as amended by the Superfund Amendments and Reauthorization Act of 1986 [SARA]) requires ATSDR, among other things, to conduct public health assessments of a hazardous waste site within 1 year of that site's proposal for the NPL.

ATSDR, in Atlanta, Georgia, is an agency of the U.S. Department of Health and Human Services. Public health assessments are one part of the process ATSDR uses to review environmental and health outcome data--as well as community health concerns--to determine possible adverse health effects. In addition, this public health assessment recommends actions to reduce, prevent, or more clearly identify site-related actual or potential adverse health effects.

A. Site Description and History

The Terry Creek site comprises four areas: two dredge spoil areas (Areas 1 and 2), a mobile home park area (Area 3), and the Hercules Outfall. The site also includes Terry and Dupree Creeks and adjacent surface water drainage areas. The Hercules facility, where chemical products (excluding, since 1980, toxaphene) are manufactured from pine resins, is not part of the proposed NPL site. These source areas and the Hercules facility are in the Atlantic coastal region of the southeastern United States, and are all east of the city of Brunswick in Glynn County, Georgia. The Terry Creek site itself is located east of Highway 17 and north of the Torras Causeway.

From 1948 through December 1980, Hercules, Inc. (Hercules was formerly known as Hercules Powder Company) produced as a major product toxaphene, a chlorinated-hydrocarbon pesticide. Toxaphene is a yellow-to-amber waxy solid that smells like turpentine[1]. It is a mixture of at least 177 significant individual compounds and is approximately 67-69% chlorine by weight. Toxaphene is produced by reacting chlorine gas with camphene, a derivative of turpentine. Hercules extracted turpentine from pine stumps or from pulp mill liquor [2]. The reaction was controlled by using a solution of carbon tetrachloride that was subsequently evaporated from the product and recycled. Hydrogen chloride and unreacted chlorine gas were absorbed in water to form hydrochloric acid. Some of the hydrochloric acid was then sold as a commercial acid and the remainder was neutralized with limestone. After 1970, the liquid waste containing toxaphene was sent to a settling lagoon EXIT. Toxaphene was adsorbed into solids, dredged from the lagoon, retained on site[2] and later deposited in off-site landfills. Toxaphene, also known as polychlorinated camphenes (PCCs), was used in the United States, primarily in the South, to control pests on cotton and other crops. In 1982 the use of toxaphene was restricted, then in 1990 was banned in the United States [1]. Through 1989[3] Hercules used Terry Creek as a navigational channel for transporting raw materials such as pine stumps. Terry Creek merges with the Back River, which empties into St. Simons Sound and the Atlantic Ocean.

Until 1972 Hercules released large volumes of waste water containing PCC (reportedly up to 200-300 pounds of toxaphene per day) from a waste water discharge point at the confluence of Dupree and Terry Creeks [3]. In 1972 Hercules was required under the Clean Water Act to build and use a waste water treatment plant to control and minimize the amount of toxaphene discharged [4]. The toxaphene content of manufacturing plant effluent ranged from 2,332 parts per billion (ppb) in August of 1970 to 6.4 ppb in June 1974 [5].

The U.S. Army Corps of Engineers (USACE) constructed a surface impoundment (including a dual dike system) to contain spoil dredged from Terry and Dupree Creeks. In 1972[6] a dike breaching occurred in a settling basin on the plant site. The dike on the perimeter of the impoundment was originally 22 feet high, and sediment and water were deposited directly into the impoundment. As the solids settled out of the dredged slurry, water drained through three weirs and back into Dupree and Terry Creeks [3]. Breaches and discharge points have appeared in the dike throughout its history [6]. Contaminants were found 3 miles away in almost all the indigenous oysters at St. Simons Sound [3]. Contaminated oysters were also found as far as 7 miles away in Jekyll Island [24]. The USACE dredged the channel again in 1978, 1983, 1987, and 1988/1989 [4].

In 1976, Hercules received its first National Pollution Discharge Elimination System (NPDES) permit for an outfall (001) discharging to Dupree Creek. The permit restricted toxaphene to a daily maximum of 1 pound per day and a daily average of 0.5 pounds per day [3]. Toxaphene discharge was later reduced to 0.00081 parts per million (ppm). Through 1993 numerous violations of the permit were issued. The releases that occurred after 1980, when toxaphene production at Hercules had ceased, were from waste water surface impoundments and runoff at Hercules. By the summer of 1984, the toxaphene production facility at Hercules was completely dismantled [7].

In 1994 the Georgia Department of Natural Resources requested that ATSDR provide assistance in evaluating the results of residential surface soil samples collected adjacent to the Hercules facility. Nine private-residence yards on the north side of the facility (where the toxaphene waste water impoundments are located) were sampled and analyzed for toxaphene. Toxaphene concentrations ranged from 0.055 to 1.83 ppm. ATSDR concluded that these toxaphene concentrations in surface soil did not pose a short- or long-term health threat to the residents [8].

In 1995 the Brunswick/Glynn County Community Based Environmental Protection (CBEP) project began to provide a comprehensive analysis of the environmental status of the area [9]. The CBEP project is a joint effort between the United States Environmental Protection Agency (USEPA), the Georgia Environmental Protection Division (GA EPD), and other federal, state, and local agencies, and the community. The Terry Creek site is within the Brunswick CBEP project area (Figure 1). Three industrial facilities in the Brunswick area are being cleaned up under federal Superfund statutes: LCP Chemical-Georgia, Inc., Brunswick Wood Preserving, and the Hercules 009 Landfill. In addition to these Superfund sites, about 17 other potentially hazardous waste sites are in the Brunswick area (Figure 1). Where applicable, information collected for the CBEP project has been used in this public health assessment.

In addition to being part of the CBEP project, ATSDR once listed the Terry Creek site as an environmental justice site. Environmental justice is the fair treatment and meaningful involvement of all people regardless of race, ethnicity, culture, income or educational status with respect to the development, implementation and enforcement of environmental laws, regulations, and policies [10]. The Office of Urban Affairs (OUA) at ATSDR was involved at the site until 1999.

B. Site Visit

In August 1997 and January 1998, ATSDR team members for the Terry Creek site visited the area. These visits are discussed below.

Carl Blair and Laura Frazier, ATSDR team members, visited the Terry Creek site on August 5 and 6, 1997. At the Coastal Health Unit they met with Dr. Brooks Taylor, District Health Director, Jane Perry Britt, an environmental health specialist with the Glynn County Health Department, and Randy McCall, also with the Coastal Health District. It was decided that the Health Department would conduct a simple survey of the residential areas adjoining the contaminated creek areas to obtain information on the number of residents, and an indication of whether they were fishing locally.

In the afternoon of August 5, 1997, Captain Anthony Blount of the Department of Natural Resources took ATSDR representatives by boat to the Terry ~~Creek area. They observed the Riverside Development, which included about four homes along the marsh coastline of Terry Creek. The majority of~~ this subdivision is on the coastline of the Back River, a section less likely to be directly affected by dredging of Terry Creek (at receding tide, the Back River flows south; thus the contaminants would be considerably diluted when they return with the flooding tide [5] to the homes north of the confluence of the Terry Creek and the Back River). The residents use the docks on the Back River. Along Dupree Creek, the Hercules Plant can be seen in the distance, as well as an abandoned property that was formerly a paint company (Dixie Paint, later the O'Brien Corporation), and a retirement home. The main dredge spoil area is generally well-vegetated and appears to be near, or below, sea level. A dike, without vegetation on its top surface, surrounds the dredge spoil. A fisherman was also seen fishing in the Back River off the Torras Causeway.

On January 21, 1998 the ATSDR team for the Terry Creek site (Dr. Shan-Ching Tsai, Laura Frazier, Linda West, and Diane Drew) visited the Brunswick area and several area hazardous waste sites. On January 20 and 21, the team held public meetings to gather community concerns about the site. Ms. Marsha Pierce from the Glynn County Health Department drove the team by the Terry Creek site, the Hercules 009 Landfill, Altama Elementary School, LCP Chemical, Brunswick Wood Preserving, and the Georgia Pacific paper mill. She provided an overview of activities at each site.

C. Demographics, Land Use, and Natural Resources Use

Brunswick is home to both a commercial fishing port and a thriving seafood industry [9]. Many tourists visit the area for such attractions as St. Simons and Jekyll Islands. Near the Terry Creek site, in Terry and Dupree Creeks, people use small boats for recreational fishing and crabbing. Tidal marshes provide feeding and breeding habitat for migratory birds and other animals. The average tidal range (the change in water levels between high tide and low tide) is about 7.5 feet [11]. The marsh vegetation is primarily smooth cordgrass *Spartina alterniflora* and needle rush *Juncus roemerianus*.

Based on 1990 (and 2000) U.S. Census data approximately 4,837 (4,270) persons are within a 1-mile radius of the Terry Creek site (Figure 2) and a total population of 62,496 are in Glynn County. The statistics within a 1-mile radius of the site indicate about a 45 (40)% white and 53 (57)% black population. Approximately 12 (9)% of the population within a 1-mile radius of the site are children aged 6 years and younger. The nearest school, the Goodyear Elementary School, is located ¼ mile north of Area 1.

Both the Riverside Subdivision and the Terry Creek Mobile Home Park are near the site. In 1997, the Glynn County Health Department of the Georgia Department of Human Resources conducted a door-to-door survey in these neighborhoods to determine whether the residents were fishing. Staff members spoke with 36 residents living in the Riverside Subdivision, and 27 residents in the Terry Creek Mobile Home Park. Approximately 10 of these 63 residents (about 16%) indicated that they do some fishing [12]. But no information was taken on the age and sex distribution of the fishing population who answered the doors during working hours--when the survey was conducted.The percentage of the fishing population could be much higher if all of the 4,000 local residents were contacted in the survey (See comment I-7, Appendix F.)

D. Health Outcome Data

Using state or local health databases, health assessors might be able to determine whether the rates of certain diseases or causes of death are higher than expected in the area surrounding a hazardous waste site. This section identifies the relevant, available databases; their evaluation is addressed in the Public Health Implications section.

The Georgia Department of Human Resources (GDHR), Division of Public Health, Chronic Disease Prevention and Health Promotion Branch, Cancer Control Section, maintains data on mortality rates for selected cancers at county levels. ATSDR reviewed a summary on mortality rates for the period of 1988-1992 and evaluated these data in the Health Outcome Data Evaluation section. The GDHR and local public health officials were also contacted for existing aggregated, tabulated, or computerized health information sources. The state and local health departments collected vital statistics such as birth data and data on the most common causes of death, such as neoplasms (tumors) and diseases of respiratory systems. Some relevant information from these sources was reviewed by ATSDR.

The smallest geographic units for the health outcome data are at county levels. The 1990 U.S. Census reported a total population of 62,496 in Glynn County, and a resident population of 4,837 persons within 1 mile of the Terry Creek site. No computerized or tabulated health outcome data have been identified that exclusively address the small resident population near the Terry Creek site.

COMMUNITY HEALTH CONCERNS

ATSDR obtained health and environmental concerns from 63 residents living near the Terry Creek site and from community groups and leaders. Because concerns about other issues and sites were also considered relevant, community concerns were not limited to the Terry Creek site. ATSDR solicited health concerns through a mailing, public availability sessions (one-on-one sessions with ATSDR staff) and other meetings, advertising the ATSDR toll-free number, and visiting nearby residences.

In December 1997, ATSDR advertised public availability sessions to be held on January 20 and 21, 1998, and solicited health concerns via mail and phone. Residents of Riverside Development and Terry Creek Mobile Home Park were targeted, as well as other area residents near the source areas (Figure 2). Each person received notice of the meetings, and received a fact sheet on public health assessments. Information was sent to approximately 350 residences and a dozen businesses.

ATSDR held the public availability sessions (PASs) to gather community concerns on the Terry Creek site. Eighteen residents attended the PASs. Residents along Terry Creek Road were surveyed to determine their source for drinking water and whether they had any concerns about the site. Nine residents on Terry Creek Road responded.

ATSDR representatives spoke with 27 residents (the 18 residents who attended the PASs and the nine residents surveyed on Terry Creek Road) living near the Terry Creek site. Seven residents (about 26%) reported that they, or their family members, had asthma or respiratory problems. Most residents did not think their respiratory problems were related to the contaminated dredge spoil. Other health complaints of one or more individuals are summarized in the Public Health Implications section of this public health assessment.

Concerns/Questions from the Community

Below are the health concerns and questions from the community, and ATSDR's responses:

Concern: People should be informed about the health hazards of eating contaminated seafood. Due, however, to the tourism industry, notifications to the public are often limited. Additionally, some community members fish at a city dock in Overlook Park (near Lanier Basin). Is seafood from this area safe to eat? Is the seafood or fish from the area creeks and rivers safe to eat ? Have fish from the Back River been analyzed, and are they safe to eat?

Response: The public should be appraised of health hazards, particularly in an area where tourism is important. Due to the cleanup operation of toxaphene-contaminated sediments, the Georgia Environmental Protection Division, Coastal Resources Division, and the U.S. Environmental Protection Agency recommend that people refrain from fishing or swimming in all of Dupree Creek and Terry Creek north of Torras Causeway to 2 miles west of its confluence with the Back River [13]. Additionally, they recommend no more than one meal per week of silver perch (yellowtail) caught south of Torras Causeway to Lanier Basin, because of contamination with PCBs and mercury from unknown sources. Clams, mussels, and oysters in these waters are not edible, based on the National Shellfish Sanitation Program standards [13]. This ban is related to a microbiological hazard. Persons fishing in Terry and Dupree Creeks should follow the fishing regulations and consumption guidelines as outlined above and as published by the Georgia Department of Natural Resources. Based on data gaps in the current knowledge of PCC residues in fish and their toxicity to humans, ATSDR recommends that exposure to contaminated seafood from Dupree and Terry Creeks be limited.

Concern: Raw sewage is sometimes in the streets after rain storms when the system is overloaded and could contribute to health problems.

Response: Raw sewage could contribute to health problems such as diarrhea. Residents should make calls to the city or county public works department when such an event occurs. This issue should also be taken up by local health officials and citizens who wish to pursue it. A Georgia Environmental Protection Division regional office in Brunswick handles such issues (Phone: 912 2647284). The sewage problem is unrelated to the Terry Creek site.

Concern: Private wells could be contaminated by seepage EXIT▸ from Hercules. Is water from the community well at the Terry Creek Mobile Home Park contaminated? Is the water from the community well safe to drink?

Response: Private wells are unlikely to be affected by seepage from the Terry Creek Dredge Spoil Areas--the contaminants (toxaphene and metals) are held primarily by soil and sediment. Also, the concentrations of toxaphene in surface water are low to non-detectable. In September 1995, two nearby private wells and the community well at the Terry Creek Mobile Home Park were analyzed for toxaphene and metals. Toxaphene was not detected with a method detection limit of 5 ppb. The maximum contaminant level (MCL) for toxaphene in drinking water is 3 ppb. The community well should be tested with a minimum detection limit below the MCL to assure residents their drinking water is safe. No metals exceeded ATSDR health screening criteria. A trace of mercury was detected in the community well at 0.41 ppb and one private well at 0.21 ppb [14]. The MCL for inorganic mercury in drinking water is 2 ppb.

The community well at the Terry Creek Mobile Home Park is used for drinking water by some families, while others are buying bottled water. As of 2001, ATSDR received no new data for the community well. The closest municipal wells draw groundwater from the Upper Floridan aquifer (approximately 750 to 1000 feet below ground surface) and are unlikely to become contaminated from the Terry Creek site [14].

Concern: People are sent to other hospitals in Savannah, Georgia and Jacksonville, Florida, thereby affecting the health statistics reported for the area.

Response: As long as an individual gives a Brunswick address, that health outcome will be counted for Brunswick, even if they went to a hospital outside of Brunswick. Birth and death data are shared between hospitals and states.

Concern: When it rains, Hercules closes a gate to prevent contamination from entering the creeks, but runoff backs up into the community. That surface water runoff from Hercules then backs up into residential yards, and some of these yards have not been tested for toxaphene.

Response: According to Hercules, no such gate exists at the plant, and Hercules does not contribute to flooding. Hercules is unaware of any yards into which drainage is flowing or has flowed from ditches from the Hercules plant. In 1992 toxaphene in plant ditch sediment ranged from less than 0.24 to 1,300 ppm (average of approximately 262 ppm) [15]. The Georgia Environmental Protection Division required Hercules to implement a Best Management Practices Plan requiring Hercules to minimize the erosion of soil and the release of waters containing toxaphene. Site drainage is to the plant ditch (N Street Ditch, an open channel with a piped section) running primarily east to west across the site [15]. On-site ditches carry surface water runoff into outfall 001 on Dupree Creek. A pipe section on the ditch and a culvert head wall are immediately west of Highway 17 [15], and residents reported the runoff from Hercules backs up into residential yards. ATSDR recommends soil sampling for toxaphene of residential yards that receive, or have received, silty runoff from ditches on the Hercules plant site.

Concern: Because toxaphene has not been tested on humans, no one knows the levels that cause health effects. No contamination should be in the community. We shouldn't be told that certain levels of toxics are OK to have in our community.

Response: Toxaphene has caused cancers in laboratory animals. Still, there are no adequate human data to evaluate the carcinogenicity of toxaphene [1]. Therefore, toxaphene is classified as a probable human carcinogen, and human exposure to it should be kept as low as possible. ATSDR's screening level for toxaphene is based on non-cancer effects in animal testings. ATSDR, however, added safety margins of 100 times to its screening levels. These safety margins compensate for the possible discrepancy of extrapolating from animal tolerance to human tolerance, and protect sensitive human populations, such as infants and pregnant women. ATSDR also added an additional modifying factor of 3 because toxaphene can alter behavioral and functional development in offspring.

As a result of human activity, some chemical contamination is inevitable in every community. Until 1990, toxaphene was used heavily as a pesticide in the South. Residues of toxaphene were transported to widely diverse places through the global movement of contaminated air. With the sensitive instruments available at modern chemistry laboratories, scientists detected toxaphene in fish samples from the Great Lakes as well as the remote lakes of the Yukon Territory in Canada [16].

Concern: Terry and Dupree Creeks could be contaminated by the Hercules 009 Landfill.

Response: Surface water from the Hercules 009 Landfill drains northeast to Belle Point Creek, which flows into the Back River and St. Simons Sound. Dupree Creek flows into Terry Creek, which flows into the Back River. It is very unlikely (i.e., only a remote possibility) that the Hercules 009 Landfill will contaminate Terry or Dupree Creeks; Belle Point Creek does not flow into Terry and Dupree Creeks [17].

Concern: Hurricanes and other storms could spread contamination from the dredge spoil areas to areas in Brunswick and out to the Atlantic Ocean.

Response: Storms could spread this contamination. This is one of the reasons USEPA proposed the Terry Creek Dredge Spoil Areas for cleanup under Superfund.

Concern: Besides Hercules, O'Brien Corporation released chemicals into Dupree Creek.

Response: A paint manufacturing facility (O'Brien Corporation) producing latex and oil-based paint was on the property adjacent to Dupree Creek (Figure 1). Waste solvents from the production of oil-based paints, such as toluene and xylene, were disposed off site. The latex paint wastes containing low concentrations of mercury, chromium, and lead [9] were solidified and deposited in an on-site landfill. The facility reported surface water discharges in 1988 and 1989 [18]. Facility estimates for surface water discharges were ¼ pound per year for acetone, ethylene glycol, toluene, and mixed xylenes. These chemicals were also released to the air until 1990, when the facility closed [18].

Concern: Current and past air releases from Hercules have affected our community.

Response: USEPA's Toxics Release Inventory database has air release data, as reported by Hercules, from 1987 through 1995. In 1995, air releases from the stacks included carbon disulfide, methanol, methyl isobutyl ketone, and mixed xylenes. Fugitive emissions included ammonia, benzoyl chloride, hydrazine, methanol, methyl isobutyl ketone, phthalic anhydride, styrene, and mixed xylenes [18]. Historical emissions (1987-1995) included these chemicals as well as biphenyl, cumene, epichlorohydrin, ethylbenzene, hydrochloric acid, and propylene. Methyl isobutyl ketone has been consistently released from the facility and is the chemical released in the highest quantity from Hercules (from over 2 million pounds in 1987 to 807,000 pounds in 1995). Xylenes were measured in air during 1996 as part of the Brunswick/Glynn County Initiative. The maximum concentrations (approximately 8.0 micrograms per cubic meter (ug/m^3) for o-xylene and 3.3 ug/m^3 for m-xylene) were recorded at Station 3, emergency management station (EMS) directly west of the Hercules facility [18]. The levels of these two xylenes in air are far below ATSDR's screening level for total xylenes (100 ppb or 434 ug/m^3) and have no significant health consequence.

Concern: There are many upper respiratory problems in the community.

Response: Upper respiratory problems might be linked to air quality in the general area of Brunswick (see the previous response). But data are unavailable to determine whether there is an increased incidence of upper respiratory problems in the Brunswick area. ATSDR recommends further evaluation of air for respiratory irritants. Additionally, data in the Brunswick/Glynn County Initiative suggests further evaluation of air releases from Brunswick facilities is needed, based on levels of potential carcinogens such as acrolein, acetaldehyde, arsenic, carbon tetrachloride, and formaldehyde [19].

Concern: Several people mentioned lung cancer, which they attributed to smoking. Other cancer concerns were colon and brain cancers.

Response: The age-adjusted mortality rate for cancers of the colon and rectum in Glynn County was lower than the rates for Georgia and the United States generally, based on 64 cases in 5-year period (1988-1992) for this county. The mortality rate for brain cancer in Glynn County is higher than the rates in Georgia and the United States. That said, however, the brain cancers in Glynn County during this period have such a small sample size (<20 cases) the mortality rate might be unstable. The rate for brain cancer in Glynn County is higher than Camden County and McIntosh County but lower than Brantley County. Each of these three counties had only a few cases of brain cancer, but their mortality rates are unstable due to the small sample sizes.

Concern: Former workers from the Hercules Plant in Brunswick reported that on-site working conditions were unsafe and that workers were exposed to toxaphene and other toxic substances produced at the plant.

Response: This information was reported to the GA-EPD and USEPA/RCRA. They referred it back to ATSDR because, in their words, they "have no authority to investigate on-site worker safety issues." ATSDR reported it to Federal OSHA authorities for follow up.

Concern: Is eating produce from gardens near the creeks or contaminated areas safe?

Response: As long as the concentrations of toxaphene in soil of garden areas are low, produce will be safe to eat. So far, soil and sediment concentrations in residential areas have been low. Still, garden soils should be analyzed for toxaphene if contaminated dredge spoil or other toxaphene contamination is suspected.

Concern: Hercules sold compost they said was not contaminated, but some community members wonder if some contamination was present.

Response: ~~ATSDR has no data to confirm or refute the presence or absence of contamination in compost. If there are off-site areas where~~ Hercules compost was used, sampling a few of these areas to determine the presence of PCC is recommend.

Concern: Dogs near local ballfields seem to have a lot of seizures. Could pesticide usage on the fields be a contributing factor? What does this mean in terms of the safety of small children playing there?

Response: There are many possible reasons for dogs having seizures. The causes can be defined only after more information is gathered and evaluated. Besides the pesticides, young dogs that have not been vaccinated could suffer from distemper--a highly contagious viral disease that affects the nervous system and causes seizures. Any possible toxaphene poisoning cannot be evaluated without environmental data. Studies have been conducted to evaluate the response of dogs to various doses of toxaphene. They found that, for a 10-kg dog (one that weighs approximately 22 pounds), a single dose of 50 mg did not cause effects, but 100 mg of toxaphene caused convulsions. Additional dosage the following day produced salivation and vomiting. A dose of 150 mg toxaphene can be fatal to dogs [1]. Chemical effects are more likely than distemper if fatality or other symptoms of the poisoning were observed. If ATSDR receives information from Brunswick citizens regarding dogs with seizures, the data will be forwarded to veterinarians at the Centers for Disease Control and Prevention (CDC) for evaluation. Children, as well as pets, should not be in an area of recent pesticide application. Although toxaphene usage as a pesticide was banned in 1990, any currently used pesticides should also be identified.

Concern: There has not been enough soil sampling in dredge spoil area #2. More samples should be taken.

Response: USEPA is planning further soil sampling to determine those areas needing cleanup.

Concern: Several people mentioned explosions at the Hercules plant and evacuation of people near their facility.

Response: ATSDR suggests that those interested in the history of evacuations contact their local fire department for information.

Concern: Glynn County is the most contaminated county in the U.S.

Response: There are three Superfund sites in Brunswick (LCP Chemical, Brunswick Wood Preserving, and the Hercules 009 Landfill) as well as one proposed Superfund site, the Terry Creek Dredge Spoil Areas/Hercules Outfall site. There were approximately 20 potentially hazardous waste sites identified in the Brunswick/Glynn County Community Based Environmental Protection Project area (Figure 1). ATSDR, however, does not have statistics to confirm or refute this assertion.

ENVIRONMENTAL CONTAMINATION AND OTHER HAZARDS

ATSDR evaluated available environmental monitoring data to determine environmental contaminants and identify specific areas that could be of concern on, or around, the site. Comparison values, which are health-based thresholds below which no known or anticipated adverse human health effect should occur, were used to make these determinations. These values allow an adequate margin of safety. In some instances, PCC concentrations exceeded comparison and background values for the area. This health assessment, therefore, focuses on such contaminants. Other contaminants (even those not known to be site-related, such as mercury) were also evaluated if they exceeded the screening criteria. Later sections of this public health assessment contain more detailed discussions of the potential for adverse human health effects as a result of exposures to PCC. Tables containing some of the environmental data used in this section are presented in Appendix B.

Toxaphene

Toxaphene is strongly adsorbed by soil or sediments, has low solubility in water, and bioconcentrates in aquatic organisms, particularly fish and fish-eating organisms that are long-lived and do not readily metabolize or quickly eliminate the contaminant. Toxaphene is acutely toxic to fish at low parts-per-billion or high parts-per-trillion concentrations [34, 21]. Aquatic organisms (crabs, fish, etc.) and plants (such as smooth cordgrass) could mobilize PCC out of the Terry Creek area. PCC in sediment could be redistributed during storms or when adjoining channels or water flow patterns are altered. In aerobic surfacesoil, PCC concentration decreased slowly, primarily through vaporization to the air. Half-lives (the time needed for the PCC concentration to decrease by 50%) of PCC in the soils are about 10 years [1] on average. In anaerobic marsh sediments, PCC components with high chlorine contents rapidly lost some of their chlorine and became degraded products with less chlorine contents. Half lives of these daughter PCC members are unknown.

People are most likely to be exposed to PCCs near the Terry Creek Dredge Spoil site through consumption of seafood. Ingestion of soil or sediment, particularly by children, is also feasible. Thus PCC in seafood and sediment are evaluated in this public health assessment. Because it is rapidly broken down and excreted, PCC does not appear to accumulate in the human body to any appreciable degree.

Exposure to toxaphene can occur both on site and off site and through more than one pathway. Therefore, toxaphene data has been included on the Brunswick area, outside the Terry Creek site. For example, soils in Brunswick near the Hercules plant were tested for toxaphene. This information is presented in the off-site section of the report.

A. On-Site Contamination

The Terry Creek Dredge Spoil Areas/Hercules Outfall site is a 118-acre area, including creeks and adjacent surface water drainage areas. It comprises two dredge spoil areas (Areas 1 and 2), a mobile home park area (Area 3) and the Hercules Outfall. Area 1, an approximately 72-acre impoundment, is at the confluence of Dupree and Terry Creeks. It is on the other side of Dupree Creek, across from the Hercules plant. Area 2, a 58-acre impoundment, is located about 1,600 feet east of Area 1 near the Riverside Development residential housing area. Area 3, a 7-acre residential area (Terry Creek Mobile Home Park), is across Terry Creek from Area 1. It contains approximately 22 mobile homes. These areas are north of the Torras Causeway (Figures 1 and 2). USEPA's 1995-1996 sampling rationale has been to determine the presence or absence of contamination in these areas. Surface soil samples were taken at surface to 6 inches below ground surface, and subsurface samples were collected about 4 feet below ground surface [14].

In this public health assessment, Dupree and Terry Creeks are considered to be part of the proposed Superfund site. These creeks received historical PCC spills, and the potential migration of PCC from the dredge spoil areas. Historical data were also reviewed to obtain a perspective on PCC in various media [22, 23]. But PCC levels in the Brunswick area have decreased in the past 20 years, so they might not be reflective of current conditions.

Soil

The Main Dredge Spoil Area (Area 1)

The main dredge spoil area consists of contaminated sediments dredged from the bottom of Terry and Dupree Creeks. In 1972, PCC concentrations in dredge spoil in Area 1 ranged from approximately 52 to 813 ppm [23]. Soil samples were collected in September 1995 from three locations in Area 1[14]. The PCC concentrations in surface soil were 18 to 240 ppm and in subsurface soil approximately 3.2 to 430 ppm (Table 1). In some cases, the PCC concentration in surface soil exceeded ATSDR's screening levels. Thus PCC was selected as a contaminant for further evaluation in this public health assessment.

Near Riverside Development (Area 2)

In 1972, PCC concentrations in dredge spoil of Area 2 ranged from approximately 0.8 to 151 ppm [23]. Three locations in Area 2 were tested for PCC in September 1995 [14]. At these locations, PCC in surface soil averaged around 6.5 ppm (Table 1). PCC concentrations were highest (56 ppm or less) in the subsurface soil adjacent to Terry Creek.

Terry Creek Drive (Area 3)

Approximately 20 soil samples collected adjacent to Terry Creek Drive have been analyzed for toxaphene [14]. Two surface soil samples--taken in September 1995--indicated the presence of PCC at concentrations ranging from 0.68 to 9.3 ppm (Table 1). In February 1996, composite samples of surface soil were collected at 13 locations in the Terry Creek Mobile Home area. The composite samples consisted of soil from approximately three locations in each yard. In most of the samples PCC was not detected. The maximum PCC concentration detected in composited soil from February 1996 was 0.49 ppm. PCC was detected in one out of three subsurface soil samples at 1.9 ppm (Table 1).

The yards of several residences adjacent to the marsh area contained miscellaneous chemicals of unknown origin. Two yards along Terry Creek Drive contained elevated levels of polycyclic aromatic hydrocarbons (PAHs) in which benzo-a-pyrene exceeded an ATSDR comparison value of 0.1 ppm. This indicated some localized contamination of surface soil from an undetermined source.

Surface water

During receding tide, Terry Creek flows east for 1.3 miles and merges with the Back River. The Back River flows south for approximately 1.8 miles and empties into St. Simons Sound and the Atlantic Ocean [3]. At flooding tide, the water in St. Simons Sound is pushed back to the creek and river [5]. Data from 1972 indicates that PCC in surface water near Terry Creek was approximately 1.4 ppb [23]. Surface water samples were collected in 1997 but did not contain PCC above the detection level of 5 ppb. At a detection level of 5 ppb, however, indication of PCC is not anticipated based on historical records. PCC is readily absorbed through skin contact and could be expected to cause problems for swimmers. But because PCC is absorbed by soil and sediment, its present concentrations in surface water should be low. Historically, it could have posed a hazard for swimmers, particularly when effluent discharge concentrations of PCC from Hercules were highest (around 1970). That said, however, the surface water of local creeks is not being used as a drinking water source.

Low concentrations of chloroform, carbon tetrachloride, and methyl isobutyl ketone were detected at a surface water sampling location in Terry Creek [25]. Because, however, their concentrations did not exceed ATSDR comparison values for drinking water, they were not evaluated further. Some of these solvents were used in toxaphene manufacturing processes.

Sediment

Elevated concentrations of toxaphene have been found in the sediments of Terry and Dupree Creeks and adjacent wetlands. In September 1995, about 14 sediment samples from the creeks and adjacent wetlands were analyzed for toxaphene. Toxaphene was present in most sediment samples at concentrations ranging from 0.16 to 2.4 ppm. Higher concentrations (8.5 to 60 ppm) were found south of Torras Causeway on Back River, in Dupree Creek northwest of Area 1, at the Hercules outfall drainage ditch leading to Dupree Creek, and in wetland sediment upgradient of the site on Dupree Creek (Figure 3). In 1997, toxaphene concentrations in sediment of Dupree and Terry Creeks ranged from approximately 7.9 to 230 ppm [25]. The highest concentration was found near the Hercules dock in Dupree Creek. In 1998, PCC concentrations from 0.62 to 33,000 ppm were found in 31 surface (0-1 ft) sediment samples from the Outfall Ditch [38]. Their average concentration was 1,300 ppm.

Fish and other Seafood

Dupree Creek, Terry Creek, and the Back River are known fisheries and habitat for several federally endangered species such as the West Indian Manatee, Wood Stork, Loggerhead Sea Turtle, and Ridley Sea Turtle [3]. The creeks provide fishing as well as blue crab collection sites for the general public [25]. Fish species caught in nearby coastal areas include striped mullet, spotted sea trout, long-nose gar, blue angelfish, sheepshead, gizzard shad and others [27]. Fish species caught recently in Terry and Dupree Creeks include yellowtail, spot, mullet, spotted sea trout, croaker, red drum, flounder, and whiting [28]. Shellfish recently caught in these creeks include shrimp and blue crab [28]. Fishing information was gathered in a door-to-door survey with 63 residents of the Riverside Development and Terry Creek Mobile Home Park who live on or near the contaminated areas of the Terry Creek site. Approximately 16% of them indicated that they do some fishing there [12]. Thus human exposure to PCC through consumption of fish and other seafood is a likely exposure pathway at the Terry Creek site.

Historical data (1970s)

PCC concentrations in effluent from Hercules were highest in the early 1970s, prior to construction of a waste water treatment plant in 1972. Until 1972 [3] Hercules released large volumes of waste water containing PCC (reportedly up to 200-300 pounds of PCC per day) from a waste water discharge point at the confluence of Dupree and Terry Creeks.

Historically, PCC contamination in seafood was not limited to the Terry Creek area but extended to St. Simons Sound [29] and Jekyll Island [24]. Data from the early 1970s indicate toxaphene contamination of rough fish (*Fundulus* killifish), and seafood (anchovy, shrimp, oysters, and finfish) in the Terry Creek area [23, 24, 30]. Some data on PCC levels in the rough fish (killifish or *Fundulus heteroclitus*) is shown in Table 2. Averages for PCC in *Fundulus* between 1970 and 1972 were around 50 ppm. In 1972 PCC in anchovies usually averaged around 10 ppm, with the maximum concentration reported being 236 ppm in 1970. Eight samples taken in 1973 and 1974 revealed anchovies in the Terry Creek area having an average PCC concentration of 2 ppm, whereas shrimp samples from the same time period showed less than 2 ppm [5]. The toxaphene concentration in white shrimp in Terry Creek was usually around 10 ppm or below in the 1970s [23]. Oysters taken from Terry Creek between 1967 and 1970 contained approximately 13 ppm PCC [24]. In 1971, oysters in the Back River at Torras Causeway contained an average of approximately 2.6 ppm toxaphene [30]. In 1972, however, the concentration dropped to 1.3 ppm [23].

Recent data (1995-1998)

Although the focus of recent data has been on finfish and shellfish, no data are available for recent PCC levels in oysters. Presently, oysters are neither harvestable nor edible near the Terry Creek site because of bacteria, and because of the lack of chemical information resulting from their omission from the sample collections (R Manning, GA DNR toxicologist, personal communication, September 8, 1997). Oysters, clams, and mussels are not harvestable and are under a shellfish ban as established by the National Shellfish Sanitation Program. This ban, which is not linked to the Terry Creek Dredge Spoil Site, extends to areas such as St. Simons Sound.

In October 1995, Hercules conducted an assessment to determine whether toxaphene discharges were affecting the edibility of fish and crabs in Terry and Dupree Creeks, adjacent to their facility [27]. Composite tissue samples were collected at one station for spotted seatrout and at four stations for blue crab. Toxaphene was not detected in either fish fillets or crab meat in any of these samples. The detection limit was 50 ppb for blue crab and 250 ppb for spotted sea trout. The USEPA guideline is a 100-ppb screening level for no further action. This sampling effort garnered only one fin fish sample, from the furthest sampling station. The sampling goal for mullet was not met.

In February and March 1997, USEPA and the Georgia Environmental Protection Division (GA EPD) collected seafood samples from Terry and Dupree Creeks as part of the environmental sampling effort to support a clean-up decision. The samples provided some evidence that organic constituents similar to those found in toxaphene were detected in fish. The estimated PCC concentrations ranged from 1.9 to 27 ppm in forage fish samples (primarily *Fundulus heteroclitus*, a nonedible rough fish) and 1.6 to 3.9 ppm in four consumer fish samples. No substantial signs of metals were detected in fish. PCC concentrations were highest in fish at the Hercules effluent channel. Analyses of blue crab tissue (meat) indicated no substantial signs of organic or metal contamination [25].

In April 1997, the GA EPD collected 59 composite samples of seafood (38 finfish such as mullet, sea trout, drum and 21 shellfish such as crab and shrimp) from four areas in Terry and Dupree Creeks. GA EPD analyzed these samples for metals (e.g., mercury), PCBs, and toxaphene [28]. GA EPD stated that toxaphene was not detected, and qualitatively described the toxaphene concentrations as below various detection limits ranging from

0.1 to 1.0 ppm (Table 4A). Further explanation of those toxaphene results in seafood samples is provided in Appendix D. Approximately 70% of the fish composites in the April 1997 data set contained PCB (Aroclor 1268) in low concentrations (0.04 to 0.18 ppm) [28]. PCBs were not detected in shellfish (crabs and shrimps), but, again, oysters were not sampled. Approximately 30% of the fish samples contained mercury ranging from 0.11 to 0.31 ppm. Arsenic in shellfish was about 3 to 5 ppm (Table 4B), which was within the normal range of 4-5 ppm for fish and seafood [43]. The GA EPD has requested some speciation of the arsenic to determine if a toxic form is present. No information is available for the sources of the PCBs, mercury, and arsenic noted above. Generally, arsenic in finfish, shrimp, and crab is present as arsenobetaine and other relatively nontoxic organoarsenical compounds [43, 47].

In addition to the complex composition of technical-grade toxaphene, the PCC compositions in fish differ from the reference standards, including the Hercules reference standard. The method used to calculate total toxaphene from chromatograms (e.g., total area method vs. 4 back peak method) also affects the estimated concentrations [32]. USEPA detected PCC in all four fin fish samples collected in February/March 1997 with the total area method [25]. On the other hand, GA EPD qualitatively determined that "toxaphene" was not detected in all fish samples collected in April 1997 at the same waste site, even though fin fish samples contained significant levels of unidentified components with gas chromatographic retention times within the envelope of toxaphene [48]. GA EPD stated that "a match for toxaphene was called if the retention times and peak ratios in the latter half of the chromatogram matched an analytical standard of toxaphene. No hits were called in any of the fish samples"[48]. No detailed description on methodology was provided in GA EPD's draft release [28].

ATSDR formally received from USEPA the August 14, 1997 analytical protocol, of which the last- 4-peak method was intended to be used by USEPA and Hercules, and, probably, the GA EPD to analyze for toxaphene.ATSDR's concerns regarding toxaphene analyses are explained in Appendix D. ATSDR will continue to evaluate toxaphene monitoring data as it becomes available. USEPA is conducting similar evaluations and improving methods for quantitative evaluation of PCC.

In April 1998 ATSDR secured the services of Dr. Mahmound A. Saleh from Texas Southern University. His expertise was requested in estimating the total toxaphene concentrations in seafood samples from hard copies of the April 1997 chromatogram data. Appendix E contains Dr. Saleh's report. Based on the GA EPD data (mainly the hard copies of GC chromatograms), Dr. Saleh concluded that toxaphene is present at concentrations below 1 ppm in most fish samples. Nevertheless, he recommended more confirmation to prove the existence, and level of toxaphene concentrations in fish (Dr. Mahmound Saleh, personal communication, November 12, 1998). The fish with estimates of toxaphene ranging from 0.5 to 1 ppm were spot, flounder, croaker, and spotted sea trout from Dupree Creek, spot from lower Terry Creek, mullet and croaker from Terry Creek at the bridge, and spot from Lanier [33]. Recently, GA EPD and the Skidaway lab made a second analysis of the April 1997 fish samples for individual PCC components with gas chromatography-electron capture detector(GC-ECD) and the specific instrumentation of gas chromatography-mass spectroscopy. The total PCC (the sum) concentration up to 26 ppm was reported (6/19/2000) for mullet. ATSDR will assess this new data in a later health consultation.

In a 1997 study by the Skidaway lab, PCC levels up to 1.2 ppm were found in the whole body of grass shrimp *Palaemoletes pugio* at this site [49]. In August 1970 [30] the PCC concentration in shrimp was 3.0 ppm.

In November 1997 [26] rough fish (*Fundulus*) and sediment samples were collected from Terry and Dupree Creeks, and the compositions of the PCC residues in these samples were qualitatively determined. Only half a dozen PCC congeners were detected in the GC-MS chromatograms. Probably, a relatively small number of PCC congeners remained in the sediments and killifish in this site. The highest number of PCC congeners were found in Dupree Creek near the dock at the small lagoon draining the dredge spoil island (Station 4), and from the plant's discharge cooling water canal or Hercules Outfall (Station 7) [26]. Quantitative estimates for total PCC levels were not performed in the November 1997 samples.

B. Off-Site Contamination

PCC is found in the Brunswick, Georgia area environment near the Hercules facility. The areas discussed in this section are not part of the Superfund site. Historical data indicates that PCC in oysters abated with distance from Terry Creek site. In the 1970s, PCC concentrations were 54 ppm at Terry Creek, 7.5 ppm at St. Simons Sound, and 1.0 ppm at Satilla River [24].

Biota: Fish

Fish samples analyzed in 1997 by Skidaway Institute of Oceanography showed PCC in liver and egg samples (fatty organs that are the best accumulators of PCC) from fish (sea trout, red drum, croaker, and flounder) caught in Dubignons Creek off Jekyll Island and in Purvis Creek, near the LCP site in Brunswick [34]. Components of toxaphene were detected and confirmed in fatty organs of fish using state-of-the-art methodology (i.e., gas chromatography with electron capture detection, and mass spectrometric detection). Estimated toxaphene concentrations were 0.5 to 1 ppm on a lipid basis or 0.02 to 0.1 ppm wet tissues in fatty organs of the off-site fish. The small mullet fingerling (whole fish) and whole grass shrimp contained less than 0.01 ppm of total toxaphene. Sea trout eggs were also collected from the Skidaway River on the northern Georgia coast to serve as background control. Total toxaphene (on a wet weight basis) from the ova of sea trout from Skidaway River area was also below 0.01 ppm, the detection limit.

Plants and Produce

Vegetables in residential gardens have not been sampled and analyzed for toxaphene. Yet historical data indicates that the thin leaf blades of smooth cord grass in the salt marsh retained a toxaphene level as high as that in the sediment (about 30 ppm on the basis of dried leaf weight). The seed had a moderate toxaphene level and the root system was relatively clean [23]. In sea water, toxaphene labeled with radioactive chlorine-36 was readily picked up through the roots by the stems and leaves of the smooth cord grass [5]. The leafy vegetables in residential gardens could be contaminated if the cordgrass experience is applicable to leafy vegetables in contaminated local gardens.

Soil

Residential yards near the Hercules Brunswick Facility

In 1995 and 1996, residential yards in the vicinity of the Hercules Facility were sampled for toxaphene. Forty samples were collected to determine whether any off-site toxaphene concentrations are associated with the facility [35]. Although toxaphene was not detected in most of the yards, eight yards were found to contain toxaphene concentrations ranging from 0.9 to 2.6 ppm. Newfields, Inc, a Hercules contractor, concluded that from a statistical analysis of these data, no pattern or trend of toxaphene dispersal from the facility was discernable.

In December 1996, residential yards in the vicinity of suspected sources of contamination were sampled as part of the Brunswick Community Based Environmental Protection Study. Thirty-four locations were sampled for toxaphene, which was found in three yards. Two of these yards had concentrations around 10 ppm (14 ppm on Stonewall St. and 9.1 ppm on Cook St.).

~~These results indicate some localized toxaphene contamination. Most of the soil samples from yards sampled between Fourth St. and Gloucester St.~~ indicate that toxaphene could be present at levels ranging from 0.36 to 1.5 ppm.

Schools

In April 1996, soil samples were collected by GA EPD from several schools in Glynn County (Glynn Academy, Jane Macon Middle School, Risley Middle School, and the Risley Learning Center) and tested for toxaphene. No toxaphene was detected [36]. In June 1996, USEPA collected soil samples at nine elementary, three middle schools, and 10 parks in the Brunswick area. Goodyear Elementary (the school closest to the Terry Creek Dredge Spoil site) was also sampled. ATSDR reviewed the June 1996 soil data and concluded that contaminants are not at levels of public health concern [36].

In November 1996 [37] an environmental consulting firm conducted further soil sampling at Burroughs-Molette and Goodyear Elementary Schools. Although no toxaphene was detected using the characteristic peak method, toxaphene was quantified using a total area method. The total area method indicated possible degraded or weathered toxaphene-like compounds averaging less than 2 ppm.

Air

Inhalation exposures to PCC are possible through volatilization of PCC in contaminated water or soil[39]. Inhalation exposures could have occurred during production of toxaphene at Hercules prior to 1980. PCC can be transported long distances in the air if it is adsorbed by particulate matter (dusts). The half-life is approximately 5 days for the vapor phase [39]. The particulate form, however, is resistant to degradation [1]. For the airborne PCC mixture, the atmospheric residence time is about 46-70 days [1].

During March and April 1996 [19] GA EPD collected air data for the Brunswick/Glynn County area from ARCO, Brunswick College, Emergency Management Station (on the Hercules plant), Georgia State Patrol, Jekyll Island, and St. Simons Island. Air samples were analyzed for toxaphene, but none was detected [19]. Data in the Brunswick/Glynn County Initiative suggest, however, that based on levels of potential carcinogens such as acetaldehyde, arsenic, carbon tetrachloride, and formaldehyde [19], further evaluation of air releases from Brunswick facilities is needed.

C. Quality Assurance and Quality Control

The limited available data used in this assessment originated from various sources over a span of more than 25 years. A wide range of data quality exists. Some reports were peer-reviewed and published in open literature, while other reports were internal publications. Some 1990s reports were formal, with detailed information in each part of the text, while other reports were in the form of draft releases, which provided raw numbers without using the formal format. There is huge uncertainty in some data sets relevant to contaminants at this waste site. ATSDR reviewed the available database and looked for any PCC mixture or individual PCC compound that could represent a potential health hazard to the public. It should also be noted here that historical data were gathered primarily for ecological studies, while current data have been collected to help USEPA determine remedies for site clean up.

Although many PCC components have now been identified and reference standards for about 20 PCC congeners are commercially available in the market [33], PCC analysis in environmental samples remains a developing field. PCC levels had been estimated by calculating the sum of selected peaks, the sum of all individual peaks, or the total area in the GC chromatogram. Because PCC is a complex mixture, it can be difficult to compare environmentally degraded and transported PCC with toxaphene standards or source materials. Even the standard references for toxaphene from various suppliers in the market differ in their compositions. Additionally, environmental processes such as translocation and transformation can, over time, change the PCC composition in environmental media. The specific processes include selective biota (e.g., *Spartina alterniflora* in the marsh) uptake, translocation or both, and atmospheric transformations, as well as benthos or sediment transformations or both (e.g., anaerobic dechlorination in the marsh sediment). These processes can affect the congener distribution. And in comparison to the Hercules toxaphene standard, they generally shift the pattern of PCC toward lower (fewer chlorines) chlorinated toxaphene components. Thus particularly when toxaphene concentrations are low, the method of analysis assumes great importance.

For the April 1997 data reviewed by Dr. Saleh, the hard copies of chromatograms indicate accurate analysis, and acceptable recovery and QA/QC criteria. Nevertheless, for future analyses of toxaphene in fish, methods other than GC-ECD have been recommended (Appendix E) [33]. Information on the efficiency of sample extraction and detailed experimental procedures were unavailable in the data package for Dr. Saleh's review. Recently the earlier, April 1997 fish samples were analyzed again at Skidaway lab with efficient procedures and advanced instrumentation. PCC content up to 26 ppm was found in mullet. ATSDR will assess these new data in a later health consultation.

The recent fish samples were limited to the February/March 1997 samples and the April 1997 samples. The fish data from other times of the year are unavailable, and the seasonal fluctuations of PCC residues in fish are unknown. During the Memorial Day holiday (5/28/2001), croakers and whiting were caught with rod and line in this area by local anglers. On that day, an ATSDR staff (S.C. Tsai) made an unofficial visit to the site and spoke with the anglers.

D. Physical and Other Hazards

USEPA is undertaking a removal operation to reduce areas of high PCC concentration in the creeks. Heavy machinery will be moving around at this site. Therefore, physical hazards commonly seen at construction sites are expected. Some type of restriction to exclude public access to the site during removal and remedial operations will be put in place.

E. Review of Potential Sources of Contamination

Possible facilities that could contribute to environmental contamination in the Terry Creek area in Brunswick had to be identified. To accomplish this, ATSDR staff members reviewed information in the Brunswick/Glynn County Community Based Environmental Protection (CBEP) Project and in USEPA's Toxics Release Inventory (TRI) database.

Community Based Environmental Protection (CBEP) Project

In several areas in Brunswick, other than the Terry Creek area, toxaphene is concentrated on site. These sites include the Hercules Plant, the Hercules 009 Landfill, the 4th Street Landfill, the T-Street Landfill, and the Old Sterling Landfill. Clean-up levels were 0.25 ppm for residential soils near the Hercules 009 Landfill. Toxaphene is present in low concentrations in most areas in Brunswick due in part totoxaphene's historical release and its possible use as an agricultural chemical. Hercules was the only manufacturer of toxaphene in coastal Georgia [17]. Although the use of toxaphene in the U. S.[1] was restricted in 1982 and banned outright in 1990, the PCC residues remains in this site as a result of Hercules' previous discharges of PCC wastes into Dupree Creek.

Toxics Release Inventory (TRI)

To identify possible facilities that could contribute to the environmental contamination in Brunswick, ATSDR staff members searched the 1987-1995 files of the TRI databases for the area around the site [18]. USEPA developed a TRI from chemical release information provided by industries for air, water, and soil. Two zip codes were searched for information in Glynn County near Terry Creek--31520 and 31521. For zip code 31520, five USEPA-regulated facilities in the TRI database were found: Brunswick Wood Preserving Co., Hercules Inc. (Gum and Wood chemicals), King & Prince Seafood Corp., LCP Chemicals, and Rich-Seapak Corp. For zip code 31521, three USEPA-regulated facilities were in the TRI database: Georgia Pacific Corp (Union St), Georgia Pacific Corp (W. 9th St), and O'Brien Corporation (Manufacturing Paints and Allied Products). With the exception of Hercules, no toxaphene source was found among any of these facilities for the period 1987-1995.

PATHWAYS ANALYSES

This section presents evaluations of the possible environmental pathways that help determine whether individuals have been, are being, or will be exposed to site-related contaminants. Environmental pathways can be completed or potential. A completed pathway indicates that human exposure to contaminants has occurred in the past, is occurring, or will occur in the future [41]. A potential exposure pathway indicates that human exposure to contaminants could have occurred in the past, could be occurring, or could occur in the future. An exposure pathway can be eliminated from consideration if exposure has never occurred and never will occur. Tables presenting completed and potential exposure pathways for this site are in Appendix C.

A. Completed Environmental Exposure Pathways

Seafood

Persons are most likely to be exposed to toxaphene near the Terry Creek site through consumption of seafood. Terry and Dupree Creeks are used for recreational fishing and crabbing, and those eating seafood from this area are likely to have been exposed to PCC through ingestion of contaminated seafood.

B. Potential Environmental Exposure Pathways

Air

The air pathway is not likely to be a problem at this site. Still, past exposures could have resulted via air when the facility was manufacturing--and consequently releasing--toxaphene to the outfall. Additionally, some exposure through air could have occurred during dredging of contaminated sediments. Historical monitoring data for toxaphene in air are, however, not available.

Soil/Sediment

Anyone, but particularly children, could accidentally ingest soil or sediment contaminated with PCC. But the Terry Creek contaminated areas are adequately vegetated, and the main dredge spoil area is remote, being accessible primarily by boat. Thus it is unlikely that low-level exposure to PCC in soils would cause harm to humans. Nevertheless, the soil is considered a potential exposure pathway because some contamination is present in residential soils and ingestion could possibly occur.

Produce from gardens

PCC may accumulate in produce (particularly leafy vegetables) grown in PCC- contaminated soils. Studies conducted during toxaphene's initial registration indicate that toxaphene is unlikely to be taken up by fruits or leafy vegetables. But many factors affect the uptake of toxaphene residues in soils. Organic carbon (log Koc = 2.47 - 5.0) and clay minerals in soils have a strong affinity to toxaphene, rendering it less available to plant absorption through interstitial water in soils (or sediments). Air movement over the plant leaves also favors the uptake of water and PCC in water solution. In addition, the composition of the sedimentary PCC residues can affect the plant uptake. *In situ* data indicated that smooth cord grass in the local marsh contained as much PCC as is found in the sandy sediment of a windy seashore [30]. In an environmental chamber experiment with Cl-36-tagged toxaphene in sea water, the bioconcentration factors were found to be 0.67, 0.58, and 0.067 for cord grass roots, stems, and leaves, respectively [5].

That said, however, the concentration in produce will still be dependent on the concentration in the soil. So far, soil and sediment concentrations in residential areas have been low. As long as the concentrations of PCC in soil of garden areas are low, produce will be safe to eat. Garden soils should be analyzed for PCC if contaminated dredge spoil or other PCC contamination is suspected.

Surface water

Toxaphene is adsorbed by soil and sediment (log Koc = 2.47-5.0); thus its concentration in surface water should be low. Toxaphene is also readily absorbed through skin contact. Currently, surface water is not thought to pose a hazard for the occasional swimmer or water skier. Historically, however, it could have posed a hazard for swimmers, particularly when effluent/discharge concentrations of PCC from Hercules were highest (around 1970). It should also be added that presently, the surface water of local creeks is not being used as a drinking water source.

Groundwater

The relatively low solubility of toxaphene in water and its strong adsorption by soil or sediment particles minimizes the leaching of toxaphene into groundwater. The private wells to the northwest of the Terry Creek Dredge Spoil areas are deep, drawing water from greater than 200 feet below land surface [45]. In addition to the deep private wells, drinking water near the site is supplied by the City of Brunswick Water Department. Its closest well is approximately 4000 feet to the northwest [45]. Additional information, however, is needed on the community well on Terry Creek Drive--residents use this water for drinking purposes. And data on groundwater contamination at the Hercules plant is also needed because it could contribute to contamination in surficial (shallow) aquifers.

PUBLIC HEALTH IMPLICATIONS

A. Toxicologic Evaluation

Introduction

PCC in fish and surface soils is the major concern for human exposure from the Terry Creek /Hercules Outfall site. Other contaminants from unknown sources in the general area include PCBs, mercury, arsenic, and numerous air contaminants. The air contaminants include acetaldehyde, arsenic, carbon tetrachloride, and formaldehyde [19]. Evaluation of the air emissions was not conducted because they were not site-related and are currently under evaluation by the State of Georgia Environmental Protection Division (GA EPD).

Discussion of the Possibility of Health Consequences

Health assessors determine possible health consequences by comparing a chemical exposure to epidemiologic evaluations of human exposures to that chemical. If assessors do not have valid human data, they use information from properly conducted animal studies. The type of data used for an evaluation is indicated for each chemical. Usually, there is little or no information on how much exposure is actually occurring at a site. So, to ensure that the public health is protected, it is assumed that maximum exposure has taken place. If, on the other hand, there are valid data on exposure of area residents to site contaminants, these will be used to decide whether an ongoing public health hazard exists.

Site-Related Contamination

Toxaphene

PCC can reach area residents, especially subsistence anglers, mainly through consumption of fish. Ingestion of contaminated surface soils and sediment is another way area residents can be exposed to PCC. PCC can also enter the human body through skin contact.

Historically, oysters containing up to 54 ppm of PCC have been reported. But in 1972 the PCC levels were reduced to 1.3 ppm. Current PCC concentrations in oysters are unavailable. Still, because of sanitation problems, oysters are not harvested in this coastal area. Killifishes--resident rough fishes--accumulated 50 ppm of PCC in the past and currently report up to 27 ppm. In past decades, migratory food fish revealed up to 35.6 ppm, but few current quantitative estimations of PCC concentrations in food fish are available for this site. The current on-site concentrations are 3.9 ppm or less, based on semi-quantitative estimations on a limited number (four) of fish samples that were available in 1998.

To determine the potential for any human health risk resulting from consumption of PCC-contaminated fish at the Terry Creek site, ATSDR has selected a screening level of 0.001 mg/kg/day. The level is based on the ATSDR's intermediate oral Minimum Risk Level (MRLi)[1]. The MRLi is the screening level below which non-cancer health effects are unlikely to occur after an intermediate exposure period of 15-364 days. Safety and modifying factors have been incorporated into the MRLi to ensure that sensitive populations, such as pregnant women, nursing mothers, infants, and children are protected.

Because a suitable chronic NOAEL or LOAEL value for the MRL derivation could not be identified in the available literature [1], ATSDR has not derived a chronic duration MRL. ATSDR's chronic MRL is the counterpart of USEPA's reference dose (e.g., the proposed RfD value of 0.00025 mg/kg/day for toxaphene.)

The dose of PCC to a hypothetical angler (weighing on average 70-kg or approximately 154 pounds) who eats 30 grams of fish a day (one fish meal of 210 grams a week or an average of about one ounce per day) is estimated to be 0.002 milligrams per kilogram per day (mg/kg/day), assuming the fish fillet contained 3.9 ppm of PCC. But this estimated dose could be 10 times higher if historical data are taken into account for the dose estimation. This hypothetical angler is also expected to receive an estimated dose of 0.0003 mg/kg/day of PCC from surface soil if they ingest 100 mg of soil similar to the soil at Area 1, or at Hercules dock--which contains about 240 ppm of total PCC.

The combined dose of PCC from fish and soil ingestion is estimated to be 0.002 mg/kg/day. This dose exceeds ATSDR's screening level (i.e., intermediate oral Minimum Risk Level, or MRLi) of 0.001 mg/kg/day for non-cancer effects after short-term exposure, and it needs further evaluation. In a dose about 10 times higher, rat pups during their early development showed both inferior righting ability and retarded maturation in a swimming test. Behavior effects were also reported in the offspring of rats receiving a dose level as low as 0.05 mg/kg/day. No dose lower than 0.05 mg/kg/day of technical grade toxaphene was reported in this short-term animal study, and for rats the *no observed adverse effect level* of Toxaphene is unknown [40]. Still, retarded maturation was also observed at dose level of 0.002 mg/kg/day in rats exposed to two toxaphene components, toxicant A and toxicant B [40]. In view of the former high PCC levels and the limited data on current PCC levels in food fish, it is recommended that pregnant and lactating women avoid consuming a large quantity of seafood caught in this area. This precaution will protect the developing nervous systems of the fetus and infant from the potentially harmful effects of PCC.

Sufficient evidence has established that toxaphene can cause cancer in laboratory animals. When administered in the diet, technical-grade toxaphene increased the incidence of liver cancers in male and female mice, and thyroid cancers in male and female rats. But no adequate human data are available to evaluate the carcinogenicity of toxaphene. Only two human studies have evaluated the association between toxaphene exposure and the risk of anemia and chromosomal aberrations [20]. USEPA has classified toxaphene as a probable human carcinogen. Three other national and international organizations have assigned similar classifications to toxaphene.

Given the estimated PCC dose of 0.002 mg/kg/day from soil and fish, the 70-kg angler is expected to receive a moderate increased risk of cancer (about 2 in 1,000) if exposed to this dose level for a lifetime. Yet this estimated risk only serves as a guide for risk management--it does not mean that cancer will occur. Among the many uncertainties with this estimate are:

1. Composition of the weathered PCC in fish differs from that in technical-grade toxaphene, and the toxaphene adsorbed on soil can have different bioavailability than technical-grade toxaphene.

2. The actual suite of PCC components in fish has not yet been tested for its toxicity in laboratory animals [42].

3. Because very few reference standards are readily available in 1990s to determine the relative response of individual congeners or to match the profiles detected in fish, most estimates of toxaphene levels are semi-quantitative.

4. The estimated concentrations of PCC in fish vary with the calculation procedure. The kinds of reference standards and the peaks selected to represent toxaphene affect the estimated concentrations of total PCC.

Contamination - Source Unknown

Mercury and PCBs

Mercury found in on-site fish did not exceed the Food and Drug Administration's (FDA) action level of 1.0 ppm. The state and USEPA recommended, however, based on contamination with polychlorinated biphenyls (PCBs) and mercury, no more than one meal per week of silver perch (yellowtail) caught south of Torras Causeway to Lanier Basin.

Arsenic

Arsenic levels of 3.3 ppm in on-site fish fall within the normal range of 4 to 5 ppm for shell fish and marine fish [43]. Much of the arsenic present in fish and shellfish exists in an organic form (arsenobetaine) that is essentially nontoxic. That said, however, some of the arsenic in seafood is in an inorganic form. For example, a recent study in the Netherlands reported that inorganic arsenic comprised 0.1 to 41% of the total arsenic in seafood [44]. Analyzing area fish for organic and inorganic arsenic will resolve the minor uncertainty on the potential contamination of food fish by inorganic arsenic.

B. Health Problems

ATSDR representatives spoke with 27 residents living near the Terry Creek site. Seven persons (about 26% of the 27 residents) reported that they, or their family members, had asthma or respiratory problems. Most residents did not think their respiratory problems were related to the contaminated dredge spoil. Other health complaints of one or more individuals included allergies, headaches, swollen joints (fibromyalgia of entire body), microvascular arteriosclerosis, arthritis, nonfunctioning thyroid, lupus, and stomach problems. A few mentioned lung cancer, which they attributed to smoking, and one had concerns about colon and brain cancers. An evaluation of these community concerns has been presented in the Community Health Concerns section.

C. Children's Exposure and Health Implications

Animal testing indicates the most sensitive non-cancer end point of toxaphene are developmental effects before and after birth [1]. When pregnant rats were ~~fed a diet contaminated with toxaphene, retarded swimming ability and inferior righting responses of their offspring were observed [40]. But the~~ exposed rats eventually attained normal swimming ability. Also, when the rats took a maze test at the age of 70 days, those previously exposed to PCC components had difficulty remembering the path leading to the food. Thus to avoid potential harm to the human fetus and infants and to protect developing systems, pregnant women and nursing mothers should avoid consuming large quantities of contaminated fish and, obviously, avoid ingesting contaminated soil. Exposure to toxaphene through contaminated fish and surface soils should also be minimized in infants and young children.

D. Health Outcome Data Evaluation

The Georgia Department of Human Resources (GDHR), Cancer Control Section prepared a report on "Mortality Rates for Selected Cancers" for the period 1988-1992. The mortality rates include age-adjusted rates using the 1970 United States population as a standard. The age-adjusted mortality rate for each individual county covered residents from 0-85 years of age. The report also documented mortality rates at county levels for the overall population. Mortality data at a smaller geographical level, such as zip code, is not currently available. In 1990, 4,837 persons lived within a 1-mile radius of the Terry Creek site, representing less than 8% of the total population (62,496 persons) in Glynn County.

The age-adjusted, annual mortality rate for all cancers in Glynn County was 190.8 per 100,000 persons in the overall population. This Glynn County rate is slightly above the rate of 175.9 in the state of Georgia and 179.8 in the United States. Among the nearby counties, the rate of 190.8 in Glynn County is within the range of the rates in other counties, e.g., 179.7 for Camden County to the south, 204.1 for McIntosh County to the north, and 177.3 for Brantley County to the west. Also, because the residents near this waste site comprise less than 8% of the Glynn County population, their health status should have only limited influence on Glynn County vital statistics.

The age-adjusted mortality rate for liver cancer in Glynn County was 3.3 per 100,000, while the rate was 2.9 for the state of Georgia and 3.0 for the U.S. But only 13 cases of liver cancer were reported in Glynn County during 1988-1992, and the rates, based as they are on less than 20 cases, might be unstable. The three other nearby counties reported only three cases and also have unstable rates. Camden had a rate of 3.6, McIntosh had

0, and Brantley 0. And because of their small populations, no cases of death from liver cancer would be expected in McIntosh and Brantley Counties.

The age-adjusted, annual mortality rate for lung cancer in Glynn County was 66.2 per 100,000. That was higher than the state rate of 54.3 and the U.S. rate of 52.5. Glynn County's lung cancer rate of 66.2 was comparable to the rates of nearby counties of 57.6 in Camden, 66.4 in McIntosh, and 61.9 in Brantley. The elevated lung cancer rate is common in this region. No studies were found regarding cases of lung cancer following toxaphene exposure.

The Georgia Department of Human Resources (GDHR), Division of Public Health also provided ATSDR with tables for the "Top Ten Causes of Death by Sex-Race Group" for Glynn County. The 1987-1996 data covered residents of various age groups. The GDHR also provided ATSDR with similar vital statistics: "Leading Causes of Death, 1991," published by the Georgia County Guide-the University of Georgia-Athens. Mortality rates of total cancers and lung cancer have been evaluated in this section. Mortality rates for noncancer diseases (e.g., heart disease, stroke) in Glynn County will be compared to state and national rates once the reference data become available. ATSDR will evaluate other health outcome data when the new data become available, if appropriate.

CONCLUSIONS

1. The concentration of PCC in environmental samples, such as sediment and fish, has decreased since 1972, when PCC in effluent from the Hercules manufacturing plant was restricted. Generally, PCC in seafood has decreased from 10s of ppm to less than 5 ppm (based on available data before 1998 for estimated concentrations in limited types of seafood). But recent (June 2000) data indicated that PCC levels in food fish remained high. For rough fish, the average PCC levels in killifish fell from 62 ppm in 1970s to 7 (1.9- 27) ppm in 1997.

2. The most likely pathway for human exposure at the Terry Creek /Hercules site is through seafood. Consumption of contaminated seafood is a concern expressed by residents consuming fish caught in, or near, the Dupree and Terry Creek areas. More information on quantitative estimations of recent PCC residues in seafood from the Terry Creek area is needed, as well as more information on the toxicologic meaning of such data. Based on these data gaps, ATSDR categorizes this site as an *indeterminate public health hazard*. More information on quantitative and qualitative estimations of recent PCC residues in seafood from the Terry Creek area and on the toxicological meaning of such information will be useful. Potential for human exposure is limited at levels that would be of health concern in the other pathways such as soil, sediment, produce from gardens, or water.

3. Approximately 26% of the of the local residents who participated in the limited sampling reported that they or their family members have asthma. Health statistics with respect to this, as well as environmental data, need further investigation.

4. ATSDR will re-evaluate the health hazard at this site when new data become available. The recent fish data prepared on 6/16/2000 by Skidaway lab were published in 2001 in peer-reviewed, open literature [31]. These new data will be assessed in a health consultation scheduled for release after this health assessment.

RECOMMENDATIONS

1. Based on data gaps such as uncertainty in the PCC levels of in fish, ATSDR recommends limiting exposure to contaminated seafood from Dupree and Terry Creeks. It is further recommended that the Georgia Environmental Protection Division (GA EPD) continue evaluation of seafood and determine whether further limits or restrictions are warranted. People eating fish from nearby areas can lower their risk of ingesting organic contaminants such as PCC and PCBs by removing fatty tissue before cooking, as well as by eating small (younger) fish.

2. Due to interference from other chlorinated compounds in the fish samples and the uncertainty they cause in the toxaphene estimates, sensitive and specific methods, such as electron capture negative ion mass spectrometry (GC-ECNIMS) are recommended for the evaluation of PCC in fish and sediment. GA EPD and USEPA will employ such methods.

3. Additional seafood sampling is needed to help assure residents that fish caught in unrestricted areas near the site are safe. In addition to further seafood samples from Terry and Dupree Creeks, additional sampling in the Back River, upstream of its confluence with Terry Creek (near Riverside Development) is recommended. The following contaminants should be analyzed in seafood: PCC, heavy metals--including mercury--and PCBs.

4. It is recommended that those residential yards that receive or have received silty run off from flooding drainage ditches on the Hercules plant site be sampled for PCC.

5. Garden soils should be analyzed for PCC if contaminated dredge spoil or other major sources of PCC contamination are suspected.

6. The community well at the Terry Creek Mobile Home Park (TCMHP) should be tested with a minimum detection limit below the MCL of 3 ppb to assure residents that their drinking water is safe. ATSDR needs further information (such as the depth of the well and any sampling data) regarding the community well at the TCMHP.

7. ATSDR has requested, and should obtain, all future or additional data for Terry Creek that is currently available.

8. Based on the results of the air toxics data set collected as part of the Brunswick/Glynn County Initiative, ATSDR recommends further evaluation of air quality in the general area of Brunswick, particularly with respect to potential carcinogens and respiratory irritants.

PUBLIC HEALTH ACTIONS

Major purposes of a public health assessment include the identification of actions to protect public health, the evaluation of whether exposure is occurring or could occur, and the determination of site-related health effects. The following public health actions have been specified.

Completed Public Health Actions

Because of the cleanup of toxaphene contaminated sediments, the Georgia Environmental Protection Division, Coastal Resources Division, and the U.S. Environmental Protection Agency recommend against fishing or swimming in all of Dupree Creek and Terry Creek north of Torras Causeway to ~~2 miles west of its confluence with the Back River~~. Additionally, they ~~recommend no more than one meal per week~~ of ~~silver perch (yellowtail) caught~~ south of Torras Causeway to Lanier Basin, based on contamination with polychlorinated biphenyls (PCBs) and mercury from unknown sources. Additionally, clams, mussels, and oysters in these waters have been deemed not edible, based on the National Shellfish Sanitation Program standards (the reasons for this ban are unrelated to the Terry Creek Dredge Spoil Site).

Ongoing Public Health Actions

The recommendations in the Recommendation section should be considered as public health actions. ATSDR will work with state and federal agencies to complete these recommendations. USEPA is currently working on sediment removal plans and site remediation. The GA EPD is conducting further air monitoring and evaluation of existing air data for the Brunswick area. As one of its potential research topics, ATSDR has selected the toxicity study of PCC residues in local fish. GA EPD is analyzing a new batch of fish samples for toxaphene, and will update the fish consumption guidance in the spring of 2003.

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Five-Year Review Report

Second Five-Year Review Report

For

Hercules 009 Landfill
(EPA ID #: GAD980556906)

Brunswick
Glynn County, Georgia

February 2004

Prepared by:
US Army Corps of Engineers
Savannah District
P. O. Box 889
Savannah, GA 31402-0889

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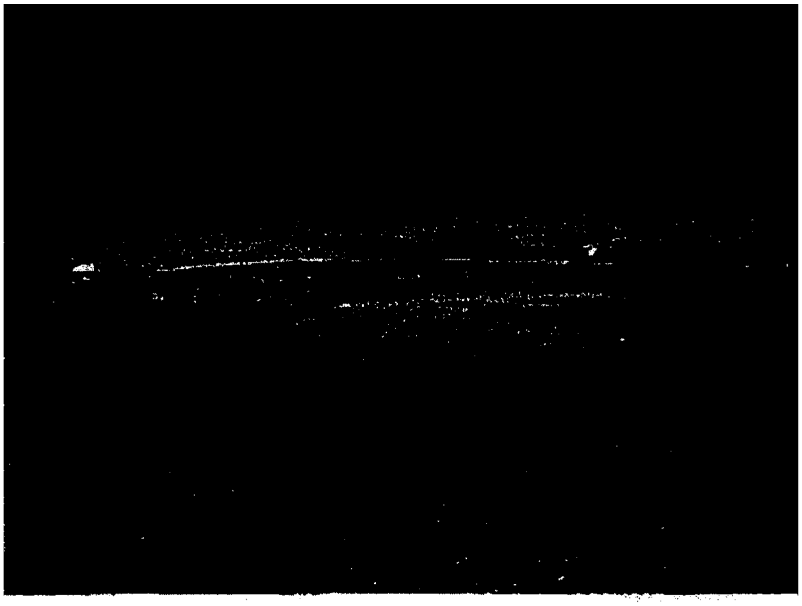
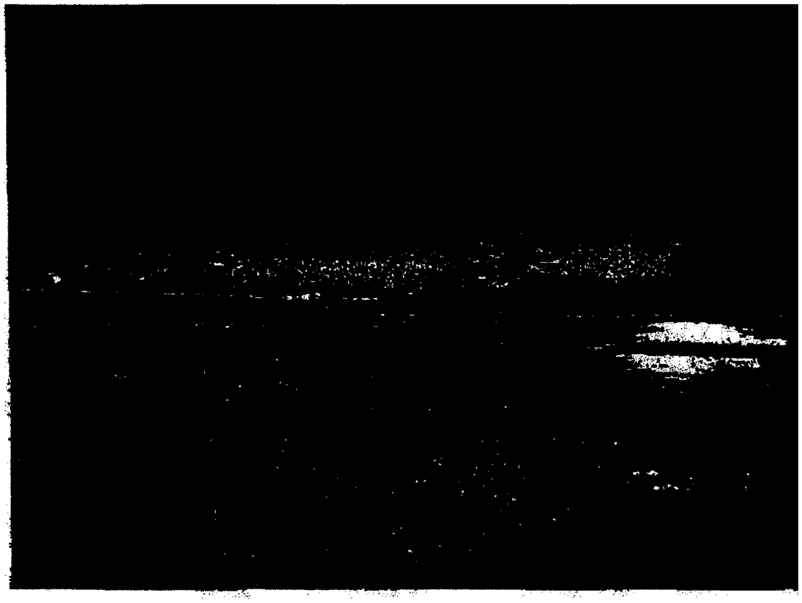
Approved by: **Date:**

Richard D. Green,
Director, Waste Management Division
US EPA, Region 4



Landfill Cover looking from the gated entrance



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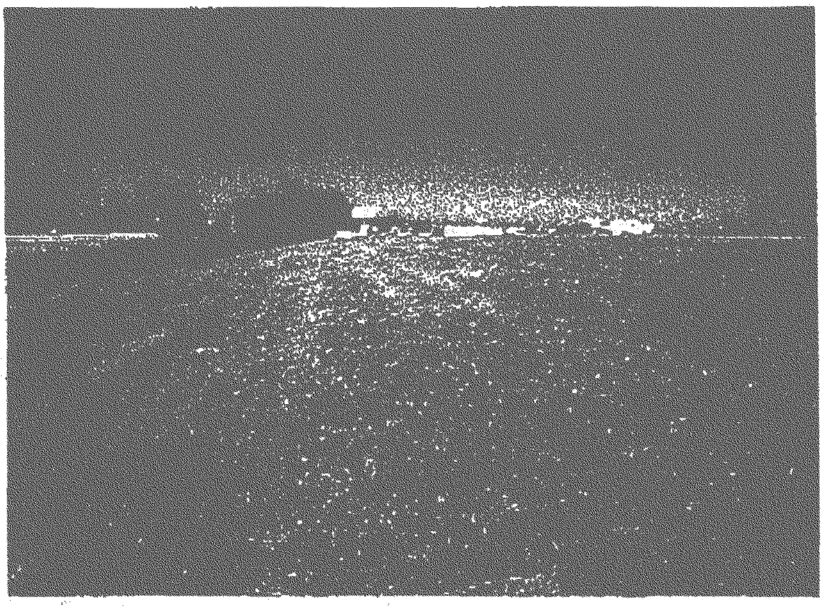
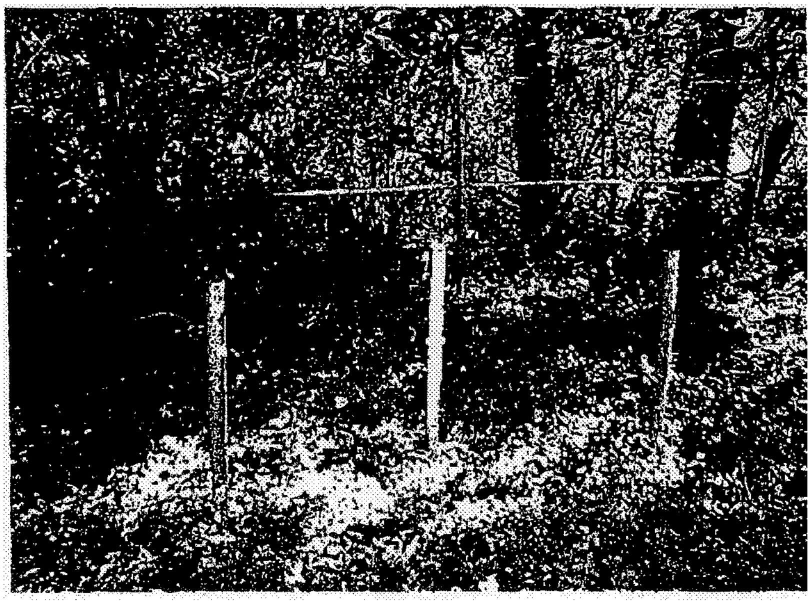


Landfill cover area requiring reseeding

Landfill cover area requiring repair

Typical ground-water monitoring well



Typical ground-water monitoring well

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Attachments

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Attachment B:	Images Documenting Site Conditions
Attachment C:	Conversation Outlines and Summaries
Attachment D:	Questions from the Glynn Environmental Coalition Interview
Attachment E:	Parlar Analysis Results

List of Acronyms

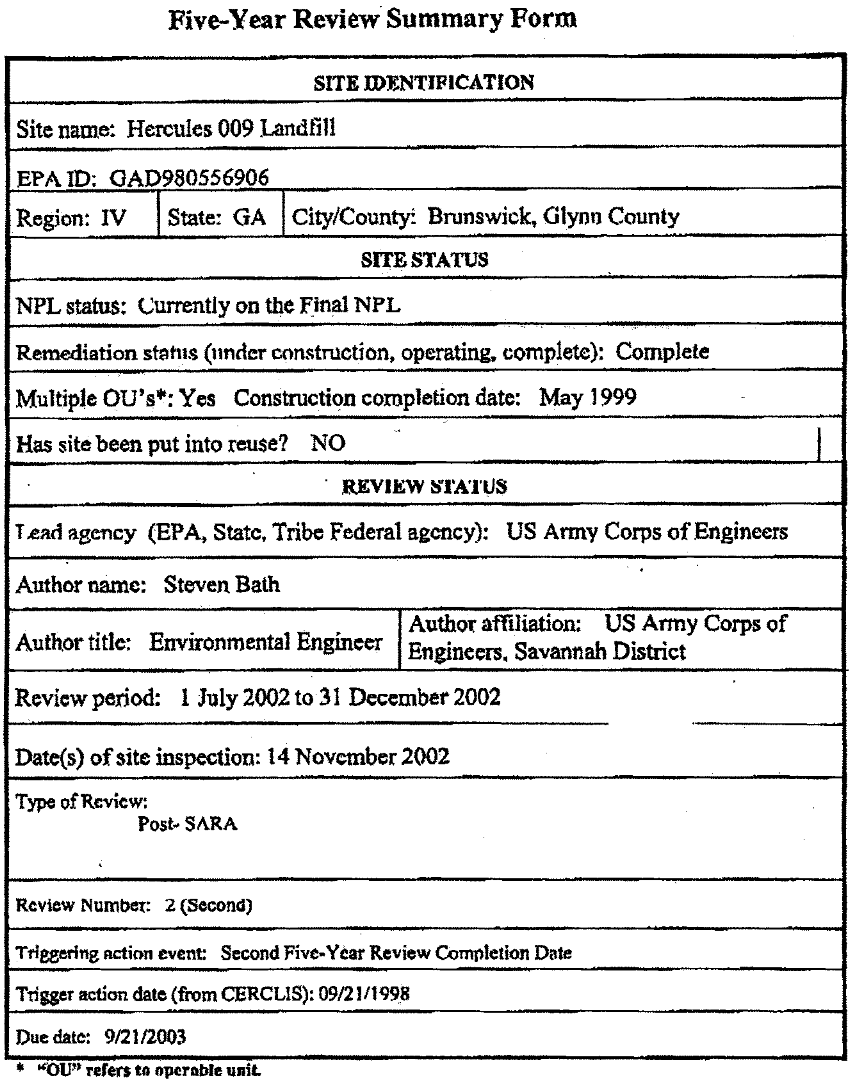
ARAR	Applicable or Relevant and Appropriate Requirement
CD	Consent Decree
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
COC	Chain of Custody
EPA	Environmental Protection Agency
EPD	Georgia Environmental Protection Division
GCL	Geosynthetic Clay Liner
MCL	Maximum Contaminant Level
MCLG	Maximum Contaminant Level Goal
MDL	Method Detection Limit
NCP	National Oil and Hazardous Substances Pollution Contingency Plan
NPL	National Priorities List
O&M	Operations and Maintenance
OUs	Operable Units
PCE	tetrachloroethene
PRP	Potentially Responsible Party
QA/QC	Quality assurance / Quality Control
RA	Remedial Action
RCRA	Resource Conservation and Recovery Act
RD	Remedial Design
RI/FS	Remedial Investigation/ Feasibility Study
ROD	Record of Decision
SARA	Superfund Amendment and Reauthorization Act
SVOCs	Semi-Volatile Organic Compounds
TCE	trichloroethene
UAO	Unilateral Administrative Order
USACE	U.S. Army Corps of Engineers
VOCs	Volatile Organic Compounds

Executive Summary

This is the second five-year review for the Hercules 009 Landfill Superfund Site. The first five-year review focused on the remedial action at Operable Unit 2 (OU2). At that time, the remedial action at OU1 was still ongoing. Currently, the remedial action at OU1 has been completed, but LTM is still ongoing. The trigger for this statutory review is the completion of the first five-year review for OU2 as shown in EPA's CERCLIS database: 21 September 1998. The five-year review is required by CERCLA because hazardous substances, pollutants, or contaminants are left on site above levels that allow for unlimited use and unrestricted exposure. All remedies have been constructed and continue to operate as intended.

The review of documents, ARARs, risk assumptions, analytical data, and site inspections indicates that the remedy at OU1 is functioning as intended by the ROD. Based on the ARAR review, there do not appear to be any regulatory changes that might impact the site for the five-year review. Sampling to date confirms the minimal contamination by technical toxaphene in the ground water. The last round of sampling showed non-detects for toxaphene.

The landfill cap appears to be in fairly good condition, requiring only minor maintenance and should continue to limit the amount of water infiltrating any remaining soil contamination. Institutional controls in the form of fencing are already in existence. However, the fencing requires maintenance to prevent access to the site since a gap in the fence was noticed during inspection. Restrictions to control future land use are to be placed on the property deed. This was required by the ROD, but remains to be done. We recommend that EPA do followup interviews with the residents to make sure that no one is still on private wells or that no one has put in new wells in the affected area. Following up on these minor recommendations will reinforce the protectiveness of the remedy.



Five-Year Review Summary Form

SITE IDENTIFICATION		
Site name: Hercules 009 Landfill		
EPA ID: GAD980556906		
Region: IV	State: GA	City/County: Brunswick, Glynn County
SITE STATUS		
NPL status: Currently on the Final NPL		
Remediation status (under construction, operating, complete): Complete		
Multiple OU's*: Yes Construction completion date: May 1999		
Has site been put into reuse? NO		
REVIEW STATUS		
Lead agency (EPA, State, Tribe Federal agency): US Army Corps of Engineers		
Author name: Steven Bath		
Author title: Environmental Engineer	Author affiliation: US Army Corps of Engineers, Savannah District	
Review period: 1 July 2002 to 31 December 2002		
Date(s) of site inspection: 14 November 2002		
Type of Review: Post- SARA		
Review Number: 2 (Second)		
Triggering action event: Second Five-Year Review Completion Date		
Trigger action date (from CERCLIS): 09/21/1998		
Due date: 9/21/2003		

* "OU" refers to operable unit.

Five –Year Review Summary Form, cont,d.

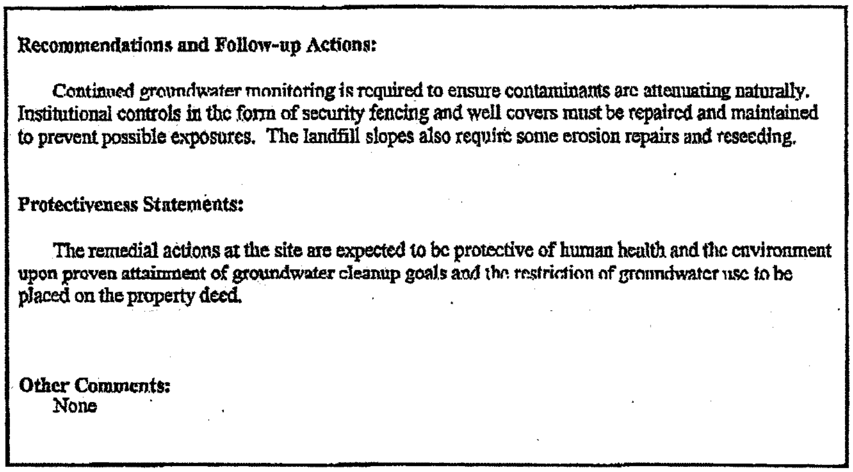
Issues:

The review of documents, ARARs, risk assumptions and analytical data and site inspections indicate that the remedy is functioning as intended by the ROD. However, concerns have been raised by Glynn Environmental Coalition (GEC) that focus on some of the decisions makde concerning the excavation of the site and the method of sample analysis. One of their main concerns was that excavation of the site might not have gone deep enough. Their concerns were based on the fact that the 0.76 ppm concentration cutoff that had been established in the ROD was not used to determine excavation depth in all areas of the landfill. If groundwater was encountered before reaching that concentration, excavation was stopped anyway. However, evaluation of the Explanation of Significant Differences (ESD), dated August 1998, provided adequate explanation for the changes made to the ROD concerning depth of excavation.

The second concern, about sample analysis, was centered around the decision to follow the Toxaphene Task Force (TTF) method. Discussions held with involved and interested individuals have helped clarify the purpose of changes made to the method used for identifying toxaphene, EPA Methods 8080 and 8081, by the Toxaphene Task Force. The analytical method itself was maximized using options available within the method. This was designed to create consistency in lab results. This is not an uncommon practice. However, the modifications to Methods 8080 and 8081 by the Toxaphene Task Force focus on identifying technical toxaphene specific to the standard used by Hercules that most closely reflects their product. Therefore, anything that did not match the reference chromatogram (i.e. off-product or weathered or biologically degraded toxaphene) would not be identified as toxaphene.

In a tiered qualification of protectiveness, using technical toxaphene as the only identifiable form would be considered the least protective. We recognize that some time was given to discussion of altered or weathered toxaphene and how to handle it. Without regulations or risk and/or toxicity studies of weathered toxaphene, options concerning responsibilities or reactions to its existence were limited. There was even some analysis done using Dr. Parlar's 22 separated congener standards. (See attachment E) Dr. Parlar is based in Germany and has been able to separate 22 toxaphene congeners into individual standards. Using this additional method for identifying toxaphene would offer the next level of protectiveness to our tiered approach. Based on more current literature concerns about the about the existence of weathered toxaphene and its possible effects holds even more merit. Identifying everything associated with toxaphene, including weathered and altered toxaphene products, would allow for the most conservative level of protectiveness. We recommend that continued investigation be done to identify or determine possible changes in toxicity information, preferred analytical procedures and verification methods, preferred standard calibration methods, and possible regulatory recommendations. We will cite four articles in the report (Refer to attachment A) that either use or recommend use of mass spectrometry as a preferred method or as a source of verification. We know that EPA is already involved in this type of research through the National Center for Environmental Assessment, as well as, other research partners. It is clear that this controversial issue will continue to be clarified as the research progresses with time.

Sampling to date confirms the minimal contamination by technical toxaphene in the ground water. The last round of sampling showed non-detects for toxaphene. The cap appears to be in fairly good condition requiring only minor maintenance and should continue to limit the amount of water from infiltrating any remaining soil contamination. Institutional controls in the form of fencing require maintenance to prevent access to the site and deed restrictions to control future land use are to be placed on the property deed



Recommendations and Follow-up Actions:

Continued groundwater monitoring is required to ensure contaminants are attenuating naturally. Institutional controls in the form of security fencing and well covers must be repaired and maintained to prevent possible exposures. The landfill slopes also require some erosion repairs and reseeding.

Protectiveness Statements:

The remedial actions at the site are expected to be protective of human health and the environment upon proven attainment of groundwater cleanup goals and the restriction of groundwater use to be placed on the property deed.

Other Comments:

None

I. Introduction

The United States Environmental Protection Agency (EPA) Region IV has conducted a five-year review of the remedial actions implemented at the Hercules 009 Landfill Superfund Site in Glynn County, Georgia. Technical support for the review was provided by the U.S. Army Corps of Engineers, Savannah District. This review was conducted from July 2002 through December 2002. This report documents the results of that review. The purpose of a five-year review is to determine whether the remedy at a site is protective of human health and the environment. The methods, findings, and conclusions of reviews are documented in Five-Year Review reports. In addition, Five-Year Review Reports identify issues found during the review, if any, and identify recommendations to address them.

EPA conducted this review pursuant to the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and the National Oil and Hazardous Substances Pollution Contingency Plan (NCP), section 300.430(f)(4)(ii). Because a remedial action was selected that allows contaminants to remain on site above levels that allow for unlimited use and unrestricted exposure, EPA is required to review such action no less than every five years after the initiation of the selected remedial action. The statutory five-year review requirement was added to CERCLA as part of the Superfund Amendments and Reauthorization Act of 1986 (SARA). EPA conducts statutory reviews when both of the following conditions are true: 1) upon completion of the remedial action, hazardous substances, pollutants or contaminants will remain above levels that allow for unlimited use and unrestricted exposure; 2) the record of decision (ROD) for the site was signed on or after 17 October 1986 (the effective date of SARA).

This is the second five-year review for the Hercules 009 Landfill Superfund Site. The first five-year review focused on the remedial action at Operable Unit 2 (OU2). At that time, the remedial action at OU1 was still ongoing. This review will also include discussion of the status of the remedy associated with OU2. The trigger for this statutory review is the completion of the first 5 year review as shown in EPA's CERCLIS database: 21 September 1998. The five-year review is required by CERCLA because hazardous substances, pollutants, or contaminants are left on site above levels that allow for unlimited use and unrestricted exposure. All remedies have been constructed and continue to operate as intended.

II. Site Chronology

Table 1 lists the chronology of events for the Hercules 009 Landfill Superfund Site.

Table 1: Chronology of Site Events

Event	Start Date	Completion Date
Discovery		11/01/1979
Preliminary Assessment		01/01/1980
Site Inspection		01/01/1980
HRS Package		06/16/1983
Proposal to NPL		09/08/1983
Final Listing on NPL		09/21/1984
NPL RP Search		08/15/1985
Admin Order on Consent		07/15/1988
RI/FS Negotiations	03/28/1988	07/15/1988
PRP RI/FS	07/15/1988	06/27/1991
Record of Decision OU2		06/27/1991
Administrative records OU2	05/14/1991	07/31/1991
RD/RA Negotiations	07/05/1991	10/11/1991
PRP RD	11/01/1991	01/07/1992
Lodged by DOJ		02/06/1992
Human Health Risk Assessment		05/01/1992
Ecological Risk Assessment		05/01/1992
Consent decree	10/11/1991	05/08/1992
Removal Assessment	12/31/1992	12/31/1992
PRP RA OU2	01/07/1992	03/03/1993
PRP RI/FS	07/15/1988	03/25/1993
Record of Decision OU1		03/25/1993
Administrative Records	08/26/1992	04/20/1993
RD/RA Negotiations	04/28/1993	08/30/1993
Lodged by DOJ		09/20/1993
Consent Decree	08/30/1993	11/29/1993
PRP RD	10/07/1993	11/17/1994
PRP RA	11/17/1994	09/29/1995
PRP RD	10/07/1993	03/02/1998
Explanation of Significant Differences		08/14/1998
First Five Year Review OU2	03/30/1998	09/21/1998

III. Background

The 16.5-acre Hercules 009 Landfill site is an inactive industrial landfill located in Brunswick, Glynn County, Georgia. Land use in the area is predominantly commercial and residential, with a shopping mall, bank, and restaurant located approximately 1,000 feet north of the site. From 1948 to 1980, Hercules manufactured toxaphene, an agricultural pesticide used to control boll weevils, ticks, and mites on cattle.

Under a State permit, Hercules used seven acres at the northern end of the property, known as the 009 landfill, to dispose of approximately 33,000 yd[3] of wastewater sludge from the production of toxaphene, empty toxaphene product drums, and toxaphene- contaminated glassware, rubble, and trash. The landfill was constructed as six cells, which reportedly were lined with a soil bentonite clay mixture across the bottom and along the bermed walls. The thickness of the toxaphene sludge disposed of in these cells was reported to be six to seven feet. Typically, the wastewater sludge was disposed of directly in the landfill; however, occasionally it was staged near the southeast corner of the landfill prior to disposal. In 1980, as a result of a State investigation that revealed toxaphene in soil and water samples from the drainage ditches around the site, Hercules' permit was canceled, and the State ordered the landfill to be closed. In 1982, EPA banned the use of toxaphene and site operations ceased.

A 1991 ROD addressed an interim action for ground water by extending the existing municipal water lines, as OU2. The second ROD in 1993, provided a final remedy for the site and addressed contaminated soil debris, sludge, ground water, and surface water, as OU1. The primary contaminants of concern affecting the soil, sludge, ground water, and surface water are VOCs, including benzene, TCE, toluene, and xylenes; other organics, including dioxin and pesticides; and metals, including arsenic, chromium, and lead.

IV. Remedial Actions

Remedy Selection

In 1991, the Record of Decision for OU2 presented the selected interim action for the site. To protect people from exposure to toxaphene and other possible contamination in the surficial aquifer, seven (7) institutional and residential locations were connected to the city of Brunswick public water supply system. The second ROD in 1993 provided a final remedy for the site and addressed contamination in the source area, including the landfill sludge, soils in the sludge-staging area, and the Benedict Road /Nix Lane area. Contamination in the ground water, surface water, sediment, and soils are treated as OU1.

The selected remedial action for OU1 includes several elements. The remediation centers on treating the consolidated surface soil, subsurface soil, and sludge using in-situ stabilization as an innovative application to treat organics. Additionally, subsurface soil and sludge from the staging area with levels exceeding 76 mg/kg of toxaphene, and surface soils from the staging area with levels exceeding 0.25 mg/kg of toxaphene were added to the landfill cells and treated. A field-scale treatability study was conducted on in situ landfill material to ensure the selected treatment method was viable. If the treatability study failed, a contingency remedy was required to treat the soil and sludge by dewatering the soil and sludge, and onsite ex-situ treatment using chemical extraction, with onsite disposal of the treated material. The treated soil and sludge in the landfill cells will be covered with a clay multi-media cover, which will be operated and maintained for a minimum of 30 years. The media selected for monitoring for COCs will include ground water, surface water, sediment, and air

A contingency remedy is required to extract and treat contaminated ground water onsite using granular activated carbon or another treatment, if toxaphene or other chemicals are shown to be migrating offsite or from their current positions, or contaminants of concern begin to increase over 50% of their current value, or it does not seem feasible that the ground water will naturally attenuate over time.

The final element of the remediation is implementing institutional controls, including deed restrictions to restrict use and access to the property. The estimated present worth cost for this remedial action is $9,900,000, which includes an estimated annual O&M cost of $104,000 for 30 years.

The major components of the selected remedy as stipulated in the Record of Decision for OU1 include:

- Conducting a field-scale treatability study and implementation of in-situ stabilization of subsurface soils and consolidated surface soils;
- Implementation of an ex-situ chemical extraction technology on the soils and sludges at the site (with onsite disposal of the treated material) in the event the treatability study concerning the stabilization of Site soils and sludges fails to meet the required standards and therefore will not be effective if implemented;
- Construction of a cover over the treated soils to reduce rain infiltration and direct contact with treated soil;

- Long-term monitoring of ground water as well as surface water and sediment in the onsite pond and the adjacent drainage ditch, with the contingency implementation of a pump and treat system in case any of the following occurs: toxaphene begins to migrate off the Hercules property; if other contaminants of concern, including benzene, are shown to be migrating from their current positions; if any levels of the contaminants of concern begin to increase over fifty percent of their current value; or in case it becomes apparent that onsite levels of contaminants in the ground water will not naturally attenuate below MCLs over time;
- Operation and maintenance of the cover for a minimum of thirty years; and
- Institutional controls for land use and ground-water use restrictions;

EPA issued an Explanation of Significant Differences in 1998. The scope of the ESD was a change in the cover for the treated soils from the landfill and off site locations. The type of cover was changed from a clay cover to one constructed from consolidated soils from the residential and drainage ditch excavations. These soils were mixed with a minimum of 3% cement and spread over the treated landfill area. EPA also changed the required depth of treatment for the contaminated soils and sludges. It was determined that treating soils below the ground water table could result in unsafe construction conditions. Contaminated soil and sludge would be treated down to the depth at which the performance standard is met or the regional ground-water table is reached, whichever comes first. All of the wells sampled (11 total) are on-site. All but 2 of the wells are clustered around the southeast corner (the down-gradient direction) of the landfill. Monitoring wells N-5 and N-7 are both on the eastern side of the landfill, near the drainage ditch that runs along the eastern boundary of the site. There are 2 shallow wells and 3 deep wells that were sampled. All other wells sampled were of intermediate depth.

Remedy Implementation

Off-Site Excavation

Approximately 8,000 cubic yards of toxaphene contaminated soils were excavated from off site locations and stockpiled onsite for treatment. Excavated areas were sampled to confirm removal of contaminated soils and then backfilled and restored to pre-excavation conditions.

EX-SITU

TREATMENT

In-Situ Stabilization

Prior to treatment activities, the landfill cells were surveyed and a grid was marked out that divided the landfill into 512 sub-cells. Each sub-cell had approximate dimensions of 25 ft. by 25 ft. square. Treatment activities occurred in up to six sub-cells at a time. The regional groundwater elevation interpolated by the Project Hydrogeologist for each treatment sub-cell was used by the remedial contractor as the targeted treatment depth. This depth was compared to the known depth of sludge. EPA was advised of cases where the known sludge depth was below the groundwater targeted treatment depth. Post remedy samples were not collected at locations where the treatment elevation is at or below the regional water table. During the in-situ stabilization, the average percentage of cement applied to the affected soils was 14.8%.

Landfill Cover

The landfill cover was constructed from soils excavated from the residential drainage ditch areas. These soils were placed on the landfill area, mixed with a minimum 3 % cement and compacted.

Long Term Monitoring

Following the stabilization of the landfill soils, ground-water monitoring is used to ensure that the concentration of COC in ground water remain below the appropriate standards.

Institutional Controls

The record of decision has been recorded with the deed in the RMC office in the Glynn County Courthouse. No records of deed restrictions controlling future access and land use were found.

Performance Standards

Chemical-specific soil excavation goals are based on attaining the baseline risk equal to or less than 1x10[-6] for future land use. The calculated goals for toxaphene include surface soil 0.25 mg/kg and subsurface soil 76 mg/kg. The cleanup goals for all of the COCs for soil and shallow ground water are shown on the following tables.

Table 2
Cleanup Goals for Surface Soil

Chemical	**Soil Action Level (mg/Kg)**
alpha BHC	0.044
Arsenic	5
Acetone	360
benzene	10
Beryllium	0.15
bis (2-ethylhexyl) phthalate	20
Cadmium	41
carbon tetrachloride	2.1
Chlorobenzene	720
Chloroform	45
Chromium III	56
copper	3,300
Dioxin/furans (TEF)	0.001
Endosulfan II	1.8
ethylbenzene	3,600
Lead	500
Manganese	4,900
Mercury	26
Methylene chloride	37
Nickel	310
toluene	7,200
TCE	25
toxaphene	0.25
Vanadium	600
xylenes	70,000
Zinc	17,000

Table 3
Cleanup Goals for Subsurface Soil

Chemical	Soil Action Level (mg/Kg)
alpha BHC	0.01
Arsenic	3,400
Acetone	1
benzene	0.06
Beryllium	61
bis (2-ethylhexyl) phthalate	46
Cadmium	11,000
carbon tetrachloride	0.07
Chlorobenzene	1.7
Chloroform	0.4
Chromium III	1,000,000
Copper	420,000
Dioxin/furans (TEF)	0.14
Endosulfan II	0.29
Ethylbenzene	13
Lead	500
Manganese	1,000,000
Mercury	3,400
Methylene chloride	0.03
Nickel	220,000
Toluene	30
TCE	0.08
Toxaphene	0.76
Vanadium	79,000
Xylenes	80
Zinc	1,000,000

Table 4
Cleanup Levels for Ground Water

Chemical	Action Level (ug/L)
benzene	5
cadmium	5
chromium	100
manganese	50
nickel	100
toluene	1,000
toxaphene	3
xylenes I	10,000

Chemical-specific ground water goals for natural attenuation are based on SDWA MCLs

V. Progress Since the Last Review

The first five-year review for the site was completed in September 1998. It was a Level 1 review and focused on the OU2 remedial action to determine if it was operating and functioning as designed and that institutional controls were in place and were protective. The remedial action at OU1 was under construction at the time of the first review and was therefore not considered in the review process. There were no recommendations or follow-up actions from the first five-year review.

During this review process, we checked with the City of Brunswick Utilities Office. We spoke to Bill Francis. He said that as far as he knows, there is no one left on private wells in this area, but that all are currently on municipal water. However, the only way to verify this with certainty would be to manually compare a listing of all customers with address listings or do a door-to-door interview of all residents on Benedict Road. We recommend that EPA do a follow-up with the residents to make sure that no one is still on private wells or that no one has put in new wells in that area.

VI. Five-Year Review Process

The purpose of a five-year review is to determine whether the remedy at a site is protective of human health and the environment. A five-year review does not reconsider decisions made during the selection of the remedy, but evaluates the implementation and performance of the selected remedy. ?

Document Review

On 23-24 July 2002, Steven Bath, and Sherry McCumber-Kahn, Environmental Engineers, with the US Army Corps of Engineers (USACE), Savannah District, met with the EPA Project Manager, Ken Lucas, and began reviewing the project files. Documents that were reviewed were related to site investigations, feasibility studies, remedial design, the RODs, construction reports, operation and maintenance plans and monitoring data. The complete list of documents is included as Attachment 1.

TF- not listed,

Data Review

The Hercules 009 Landfill EPA Site has had several sampling events performed utilizing 18 monitoring wells and 2 irrigation wells since September 1983 when the site was initially identified. Based on the data from the latest round of monitoring, November 13, 2002, one contaminant was found to be above action levels. The only two contaminants analyzed for were toxaphene and benzene. The benzene was detected at monitoring well N-5 at 0.0066 mg/L, which is just above the MCL of 0.005 mg/L. Despite being slightly above the action level there has been a marked decrease from the 1999 concentration (0.62 mg/L) detected. Natural attenuation will continue to reduce the concentration of benzene to be detected in the ground water at this site. All results for Toxaphene were non-detect. The chromatograms for this sampling event verify that no toxaphene was detected in the ground water at the Hercules 009 Landfill. Since toxaphene has a very low solubility coefficient, the concentration of toxaphene in the ground water would be expected to be very low to non-existent. Transport of toxaphene has been established to be through colloidal suspensions.

It is difficult to establish a trend of toxaphene degradation across all of the sampling events at the site for the following reason. The method used to identify toxaphene was modified in 1993 to the Toxaphene Task Force (TTF) Method. Changes in detected concentrations between pre and post TTF Method may not be representative of conditions on site but may only be a result of the different analysis and identification methods.

Site Inspection

An inspection of the closed Hercules 009 Landfill was performed by Mr. Steve Bath and Mrs. Sherry McCumber-Kahn, both with the US Army Corps of Engineers (USACE), Savannah District, on 14 November 2002. The inspection was performed concurrently with a ground-water sampling event being conducted by Mr. Bill Medlin of RMT, Inc. The purpose of the inspection was to assess the protectiveness of the completed remedy. The inspection generally included visual observation of the perimeter fencing used to restrict access, the condition of the landfill cap, and inspection of the areas immediately adjacent to landfill limits. The entire area inside the fenced boundary was visually inspected. In general, the areas inspected had good grass cover. The grass cover and the general appearance of the landfill can be seen on Photographs 1 and 2 in Attachment B to this report. However, the east slope of the landfill, closest to the Golden Isle Parkway, has several large areas with little to no vegetative cover. These areas require reseeding and maintenance to prevent possible erosion problems. Several areas of erosion were detected on the north slope of the cover. These areas are also in need of maintenance. These problem areas are visible in Photographs 3, 4, and 5 in Attachment B to this report. No undesirable vegetation was observed on the landfill cap.

The inspection of the landfill also focused on site security and integrity of the monitoring well network. It was evident that several of the monitoring wells require maintenance. Well cover hinges have rusted and broken and the majority of the monitoring wells were not labeled. On the west side of the landfill, the security fence needs maintenance and repair. A large pine tree has fallen on the fence and many areas of the fence are overgrown with vines and leaning outward. One hole through the fence was noted but there were no indications that persons had entered the site. All of the gates to the site were properly secured.

There were no observed uses of ground water in the immediate vicinity of the landfill.

The Repository at the Glynn County Public Library was also inspected to ensure the availability of the landfill documentation for the general public. The information was readily available, organized and appeared to be complete.

Interviews

Annie Godfrey, EPA Project Manager

On 6 August 2002, Sherry McCumber-Kahn and Steven Bath called Annie Godfrey, former RPM for the Hercules 009 Landfill site. Although no longer in charge of the project, She was the RPM during many of the significant actions at the site. EPA considers the project to be in an operation and maintenance phase. Remediation of the landfill and surface soils is complete and ground-water monitoring is continuing. Annie was not aware of any incomplete issues for the remediation from EPA's perspective. Annie recommended we interview Lavon Ravells for any questions concerning the laboratory analysis of toxaphene.

Lavon Revells, Lead Chemist, EPA Region 4 Pesticide and PCB Laboratory

On 28 October 2002, Sherry McCumber-Kahn and Steven Bath conducted a phone interview with Mr. Lavon Revells, Lead Chemist for EPA Region 4 Pesticide and PCB Laboratory in Athens, Georgia. The purpose of the conference call was to get a better understanding of how the Toxaphene Task Force (TTF) developed the analytical method used at the landfill and how it was different from EPA Method 8081. Other topics for discussion included the degradation of toxaphene and its persistence in the natural environment. In addition, an important objective of the conference call was to establish the EPA's position on toxaphene analysis (technical and weathered toxaphene) along with its persistence and risk to human health. The Toxaphene Task Force was made up of representatives from the EPA, EPD, GADNR, and Hercules.

Keith Maruya, Associate Professor, Skidaway Institute of Oceanography

On 3 September 2002, Sherry McCumber-Kahn and Steven Bath met with Keith Maruya, Ph.D., Associate Professor, in charge of the Environmental Organic Chemistry Lab at Skidaway Institute of Oceanography. The purpose of the meeting was to get a better understanding of how toxaphene is quantified. The meeting included a discussion about the degradation of toxaphene and its persistence in the natural environment. In addition, an important objective was to establish the difference between the method developed by the Toxaphene Task Force (TTF), the standard EPA method, and the current method used by scientists in the field. The Toxaphene Task Force was made up of representatives from the EPA, EPD, GADNR, and Hercules.

Glynn Environmental Coalition

On 2 December 2002, Mike Sydow, Steve Bath, and Sherry McCumber-Kahn met with Mr. Daniel Parshley and Dr. R. Kevin Pegg in Brunswick, Georgia. Daniel Parshley is a representative of the Glynn Environmental Coalition (GEC). Kevin Pegg, PhD is a toxicologist employed by GEC as a consultant through a Technical Assistance Grant (TAG)

The purpose of our meeting was to get a better understanding of GEC's concerns. We also wanted to clearly state our mission.

Mike started off the meeting by stating our two main objectives: 1.) To remain objective within the review process; and 2.) To address as many of GEC's concerns as possible without addressing policy issues. Mike also made clear that we would not be able to answer all 129 questions presented by Mr. Parshley but that the questions would be included in our report as part of an appendix. It was established that the Corps' scope for the 5-Year Review is guided by CERCLA.

In conclusion, the objectives of the meeting were met. The Corps established its role clearly and GEC expressed their concerns openly. The main issues of concern are related to the methods established by the TTF and the fact that treatment of the site was stopped at groundwater instead of where 76 ppm contamination limit was established.

No other individuals familiar with the site and its status were interviewed.

VII. Technical Assessment

Question A: Is the remedy functioning as intended by the decision documents?

The review of documents, ARARs, risk assumptions and analytical data and site inspections indicates that the remedy at OU1 is functioning as intended by the ROD. However, concerns have been raised by Glynn Environmental Coalition (GEC) that focus on some of the decisions made concerning the excavation of the site and the method of sample analysis. One of their main concerns was that excavation of the site might not have gone deep enough. Their concerns were based on the fact that the 0.76 ppm concentration cutoff that had been established in the ROD was not used to determine excavation depth in all areas of the landfill. If groundwater was encountered before reaching that concentration, excavation was stopped anyway. However, evaluation of the Explanation of Significant Differences (ESD), dated August 1998, provided adequate explanation for the changes made to the ROD concerning depth of excavation.

WAS DONE, TS IGNORED

The second concern, about sample analysis, was centered around the decision to follow the Toxaphene Task Force (TTF) method. Discussions held with involved and interested individuals have helped clarify the purpose of changes made to the method used for identifying toxaphene, EPA Methods 8080 and 8081, by the Toxaphene Task Force. The analytical method itself was maximized and/or standardized using options available within the method. This was designed to create consistency in lab results. This is not uncommon practice. However, the modifications to Methods 8080 and 8081 by the Toxaphene Task Force focus on identifying technical toxaphene specific to the standard used by Hercules that most closely reflects their product. Therefore, anything that did not match the reference chromatogram (i.e. off-product or weathered or biologically degraded toxaphene) would not be identified as toxaphene.

No! CHANGED TO elimi- [illegible] toxaphene [illegible] By [illegible]

In a tiered qualification of protectiveness, using technical toxaphene as the only identifiable form would be considered the least protective. We recognize that some time was given to discussion of altered or weathered toxaphene and how to handle it. Without regulations or risk and/or toxicity studies of weathered toxaphene, options concerning responsibilities or reactions to its existence were limited. There was even some analysis done using Dr. Parlar's 22 separated congener standards. (See attachment E) Dr. Parlar is based in Germany and has been able to separate 22 toxaphene congeners into individual standards. Using this additional method for identifying toxaphene would offer the next level of protectiveness to our tiered approach. Based on more current literature concerns about the existence of weathered toxaphene and its possible effects holds even more merit. Identifying everything associated with toxaphene, including weathered and altered toxaphene products, would allow for the most conservative level of protectiveness. We recommend that continued investigation be done to identify or determine possible changes in toxicity information, preferred analytical procedures and verification methods, preferred standard calibration methods, and possible regulatory recommendations. We will cite four articles in the report (Refer to attachment A) that either use or recommend use of mass spectrometry as a preferred method or as a source of verification. We know that EPA is already involved in this type of research through the National Center for Environmental Assessment, as well as, other research partners. It is clear that this controversial issue will continue to be clarified as the research progresses with time.

The cap appears to be in fairly good condition requiring only minor maintenance and should continue to prevent water from infiltrating any remaining soil contamination. Institutional controls in the form of fencing require maintenance to prevent access to the site and deed restrictions to control future land use are to be placed on the property deed.

Question B: Are the exposure assumptions, toxicity data, cleanup levels and remedial action objectives (RAOs) used at the time of the remedy selection still valid?

There have been no changes in the site or surrounding properties that would affect the protectiveness of the remedy.

Changes in Standards and To-Be-Considered (TBC) Criteria

The majority of the ARARs identified in the ROD (Section 10.2) pertain to the soil remediation portion of the remedy. RCRA waste management and disposal requirements (including land disposal restrictions) as well as Clean Air Act requirements and location-specific ARARs should all have been complied with at the time the soil treatment and capping and as such are not evaluated in this five-year review. The only ARARs identified for the long term monitoring of groundwater were Federal Maximum Contaminant Levels (MCLs) and non-zero Maximum Contaminant Level Goals (MCLGs). No TBC criteria were identified for the selected remedy.

The following table lists MCL values for COCs in groundwater. Changes to a promulgated standard are highlighted in the table and the impact of the change to the remedy is discussed below.

Table 5
Changes in Chemical-Specific ARARs for Groundwater Contaminants of Concern[1]

Contaminant	Cleanup Level (ug/L)	Standard[2] (ug/L)	
Arsenic	50	Previous	50
		New	10[3]
Beryllium	4	Previous	4
		New	4
Cadmium	5	Previous	5
		New	5
Chromium	100	Previous	100
		New	100
Copper	1300[4]	Previous	1300
		New	1300
Lead	15[4]	Previous	15
		New	15
Manganese	50[5]	Previous	50[5]
		New	50
Nickel	100	Previous	100
		New	None[6]
Vanadium	Not established	Previous	None
		New	None
Zinc	5000	Previous	5000[5]
		New	5000
Acetone	Not established	Previous	None
		New	None
Benzene	5	Previous	5
		New	5
Ethyl benzene	700	Previous	700
		New	700
Toluene	1000	Previous	1000
		New	1000
Xylenes	10,000	Previous	10,000
		New	10,000
Toxaphene	3	Previous	3
		New	3
Dioxins/Furans	0.3	Previous	0.3
		New	0.3[7]

1 – Chemicals of Concern identified in Table 6-2 of the March 1993 ROD.
2 – Standards are SDWA MCLs (40 CFR 141, Subpart G).
3 – While the current MCL for Arsenic is still 50 ppb, the new MCL of 10 ppb becomes effective in 2006 and will have to be evaluated during the next five-year review.
4 – Values for copper and lead are not based upon MCLs, but rather treatment techniques (40 CFR 141.80).
5 – Values for Manganese and Zinc from the 1993 ROD are based upon the secondary MCL (40 CFR 143).
6 – The MCL for nickel was vacated on 6/29/95 (60 FR 33926).
7 – The MCL listed is for 2,3,7,8-TCDD (Dioxin).

Two MCLs have changed since the signing of the ROD in 1993. The first is for arsenic that went from 50 ppb to 10 ppb. The effective date for the new MCL is not until 2006 and therefore for this five-year review, there should be no impact. However, the MCL will be applicable for the next required five-year review and will have to be evaluated at that time.

The second change in MCLs pertains to copper. In June of 1995, the MCL for copper was vacated. It is recommended the cleanup goal for copper be left unchanged, however, as the copper MCL may be re-instated at some future date.

Question C: Has any other information come to light that could call into question the protectiveness of the remedy?

No additional information has been identified that would call into question the protectiveness of the remedy. – GW issues.

Technical Assessment Summary

The review of documents, ARARs, risk assumptions and analytical data and site inspections indicate that the data being collected seems appropriate to determine if the remedy is functioning as intended by the ROD. Recommendations have been made to do further research in response to concerns regarding existence and possible effects of weathered toxaphene.

The cap appears to be in fairly good condition requiring only minor maintenance and should continue to limit the amount of water from infiltrating any remaining soil contamination. Institutional controls in the form of fencing require maintenance to prevent access to the site and deed restrictions to control future land use are to be placed on the property deed.

VIII. Issues

Table 6

Issue	Currently Affects Protectiveness (Y/N)	Affects Future Protectiveness (Y/N)
Complete list of COCs	Y	Y
Low flow groundwater sampling is inappropriate	Y	Y
Toxaphene Task Force Modifications to Method 8081	Y	Y
Security Fencing and well covers need repairs	Y	Y
Landfill cover requires some erosion repairs and reseeding	N	Y
Deed Restrictions	N	Y

IX. Recommendations and Follow-Up Actions

Table 7

Issue	Recommendation/ Follow-Up Actions	Party Responsible	Oversight Agency	Milestone Date	Affects Protectiveness (Y/N)	
					Current	Future
Complete list of COCs	Sampling and analyses should include the complete list of COCs	PRP	EPA		Y	Y
The Toxaphene Task Force Modifications to Method 8081	Method should be reexamined in the context of more current information on preferred methods of identifying toxaphene.	PRP	EPA		Y	Y
Security Fencing and well covers	Fencing and well covers require maintenance	PRP	EPA		Y	Y
Landfill cover Erosion	Repair erosion and reseed slope as needed.	PRP	EPA		N	Y
Deed Restrictions	Place deed restriction to control future land use.	PRP	EPA		N	Y
OU2	Door to door interviews of residents on Street to verify that all are on municipal water.	PRP	EPA		Y	Y

X. Protectiveness Statement

The remedial actions at the site are expected to be protective of human health and the environment upon proven attainment of ground-water cleanup goals.

Continued groundwater monitoring using appropriate sampling and analytical methods is required to ensure contaminants are attenuating naturally. Institutional controls in the form of deed restrictions must be implemented to restrict land use and prevent possible future ground-water use.

XI. Next Review

The next five-year review for the Hercules 009 Landfill Superfund Site is required by July 2008, five years from the date of this review This review should ensure toxaphene is not detected in the monitoring well network above the required cleanup levels, by using the most current method of analysis and identification.

Georgia Department of Natural Resources
2 Martin Luther King Jr. Dr., S. E., Suite 1154 East, Atlanta, Georgia 30334
Lonice C. Barrett, Commissioner
Environmental Protection Division
Carol A. Couch, Ph.D., Director
404/656-2833

June 4, 2004

Mr. Leo Francendese
US EPA. Region 4
Atlanta Federal Center
61 Forsyth Street
Atlanta, Georgia 30303

RE: Second Five-Year Report
Hercules 009 Landfill
Brunswick, Georgia
US Army Corps of Engineers
February 2004

Dear Mr. Francendese:

The Georgia Environmental Protection Division (EPD) has reviewed the "Second Five-Year Review Report" dated February 2004 by the US Army Corps of Engineers. No deficiencies were found during our review, other than the LTM being left off of the *List of Acronyms.*

If you have any questions, please contact Nikki Fleshman at (404) 656-2833.

Sincerely,

Jim Ussery, PE
Program Manager
Hazardous Waste Management Branch

File: Hercules 009
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May 7, 2004

VIA E-MAIL & OVERNIGHT MAIL

Mr. Leo Francendese
US EPA Region IV, Waste Division
South Site Management Branch
61 Forsyth Street
Atlanta, Georgia 30303-3104

RE: **Hercules 009 Landfill Site – Brunswick, Georgia**
Hercules Comments - Second Five-Year Review Report,
Prepared for EPA by USACE February 2004

Dear Mr. Francendese:

Hercules has taken the time to review the Second Five –Year Review Report of the Hercules 009 Landfill and has significant comments on the document. The following is a discussion of these comments.

Overview

Hercules believes that the site clearly does not currently pose a risk to human health or the environment and we do not expect that it will in the future. All performance standards have been achieved for both Operable Unit – 1 (OU-1) and Operable Unit – 2 (OU- 2) Remedies. The Remedy for OU – 2 that involved the connection of local residences and a church to city water was satisfactorily completed in 1992. The Remedy for OU - 1 which involved excavation and consolidation of soils above excavation standards, stabilization/solidification of toxaphene affected soils and sludges, installation of final cover, and natural attenuation of groundwater was also satisfactorily completed in 1999. In view of the past ten years groundwater monitoring data, Hercules believes that it is appropriate to reduce the scope and frequency of current groundwater monitoring program, and install sensible institutional controls. In addition, Hercules encourages EPA to consider deletion of the site from NPL, so that a portion of the property can be returned to an appropriate and productive use.

Summary of the Remedy

Hercules believes it is appropriate to initially establish the context of our comments on the five-year review report. As described in Hercules comments on the Record of Decision for OU-2, the EPA selected remedy was extremely conservative. The following is a summary of Hercules issues with the overall Remedy.

- **Overall** –The risk management decision was extremely conservative. Apparently little consideration was given to the reduction in potential risk afforded by the OU-2 ROD which involved supplying municipal water lines to local residents and a church.

- **Carcinogenicity of Toxaphene** – We believe EPA's classification of toxaphene as a probable human carcinogen and EPA's assignment of a Carcinogenic Slope Factor of (CSF) of 1.1 $(mg/kg\text{-}d)^{-1}$ to be overly conservative.
- **Soil** - The clean-up standard for toxaphene for residential use is the lowest observed in the Superfund Program, owing to extremely conservative and unrealistic exposure assumptions. EPA's land use decision was to assume that the entire Hercules property would be used for residential use and required remediation accordingly. The site remains under Hercules control and there is little chance (if any) of it becoming used for residential.
- **Sludge** - There was no evidence of leaching of toxaphene into the groundwater or for the potential for leaching to reach unacceptable levels, yet EPA chose to stabilize the landfill when a cap would have been equally as protective at a much lower cost.
- **Groundwater** There were very few if any detections of toxaphene in groundwater and therefore there was an insufficient basis for a contingent pump & treat remedy.

Similar critiques regarding this site were specifically noted in the General Accounting Office Reports. (Improved Reviews and Guidance Could Reduce Inconsistencies in Risk Assessments GAO RCED-94-220, Risk Assessment Assumptions and Issues GAO TRCED-95-206).

General Comments on the Draft Five - Year Report

- The report goes outside the primary purpose and objectives of a Five-Year Review and inappropriately proposes a system to enhance the protectiveness of the existing remedy. We believe that this concept of enhancing an already conservative remedy is unprecedented and does not belong in an objective evaluation of the performance of the remedy. Therefore, the proposed system for a tiered level of protectiveness should be deleted from the document.

- Per EPA's Comprehensive Five-Year Review Guidance, the basic questions that are to be evaluated are:
    - What were the Remedial Action Objectives and have they been satisfied?
    - What were the Performance Standards and were they satisfied?
    - Is the remedy still protective of Human Health and the Environment?
    - Is there any new information that has impacted the protectiveness of the remedy?

- The report should be revised to strictly answer the questions posed in EPA's Comprehensive Five-Year Review Guidance.

- The report should also be revised to improve flow, structure, logic, and writing. A redline-strikeout version of the report is attached for your consideration that includes comments, notes and suggestions.

- The report is generally not well written and contains many opinions, speculative and/or unsupported statements. The report takes off on tangents that are not germane to the performance of the Remedy. Specifically, there is no connection discussed between the concern regarding the Task Force method and potential concerns regarding performance of the solidification/stabilization remedy. We also believe that the report lacks objectivity as evidenced by the direct incorporation of the GCEC's concerns into the body of the report. It is our experience on other Superfund sites that the report is an objective document and that stakeholder concerns (PRP's, community, states) are placed in an appendix, and addressed in a responsiveness summary.

- In the beginning of the report, the distinction is made between toxaphene and other forms of "toxaphene" but this distinction is not carried through the document. We suggest the report use "toxaphene" to mean technical toxaphene and "chlorinated camphene" to describe all other forms of "toxaphene".

- In the summary form and in the body of report there is a segue lacking from the second paragraph which describes the Task Force Method and the thirds paragraph which discusses tiered protectiveness.

- The chemistry and toxicity of toxaphene is much more complex in comparison to typical environmental contaminants. In discussing toxaphene, toxaphene congeners, and sophisticated analytical techniques, the report ventures into research areas and should be more accurate and precise when discussing these topics. We are concerned that the primary author of the report; The US Army Corps of Engineers, (USACE or The Corps) does not have the appropriate background and experience to evaluate the more complex aspects of these issues. Therefore, we recommend that EPA and/or EPD chemists/toxicologists at least review this discussion for technical content and accuracy.

- We suggest that the report add a recent study on the effects of weathered toxaphene. "Toxicity and Tissue Selective Accumulation of Weathered and Unmodified Toxaphene by the Mummichog (Fundulus Heteroclitus), Zimmerman, J.M., Maruya, K.A. Dioxin 2003.

- We would expect that the review team would have interviewed the residents and the church who were connected to city water and assess whether the water lines were functioning and/or being used, and perhaps assess general concerns about the site. Although it was outside the scope of the remedy, ~~it should be noted that Hercules installed a HDPE drainage culvert on the eastern side of the landfill.~~ This was done at the request of the Director of the Glynn County School Board.

Specific Comments by Section

Executive Summary

1. The report should state "Draft" Five-Year Review Report
2. The report should state that the Corps is preparing the report for EPA.
3. The ongoing groundwater sampling confirms the absence of toxaphene. The only detection of toxaphene was circa 1991 in monitoring well N-6 SR. The sample was a highly turbid groundwater sample and the analysis was performed using a defective analytical standard for toxaphene. Subsequent analyses of this well for a period of over ten years have clearly demonstrated that this result was an anomaly.

Summary of Issues

4. ¶ 1 - This paragraph should be reworded to reflect that this is the interpretation of the requirements of the ROD by the Glynn County Environmental coalition.

5. ¶ 2 - The SW-846 Methods 8080 and 8081 were not modified. Guidance was developed between Hercules, EPA and EPD chemists on how to interpret the chromatograms because neither qualitative nor quantitative guidance was available on how to measure toxaphene. The notes of the interview with Mr. Lavon Revells –USEPA also indicate that he explained the development of the Task Force Guidance to the review team.

6. ¶ 3 - As indicated in the general comments the tiered protectiveness approach is not appropriate in this document. Specific comments and concerns are included in the redline strikeout version.

7. ¶ 4 – The performance standard for groundwater is measurable attenuation of benzene that we believe has been achieved.

Recommendations and Follow-up Actions:

8. We believe that the only remaining issue in groundwater regarding the performance of the remedy in groundwater is to demonstrate that the benzene concentrations will continue to attenuate to levels below MCL. We understand that EPA may desire to monitor selected wells for toxaphene and chlorinated camphene to address GCEC concerns. We believe that this monitoring if adopted by EPA should be finite in duration and/or until a well-defined and measurable technical endpoint is achieved.

Background

9. Hercules did not operate the landfill after the GaEPD required the landfill be closed as is currently suggested by the report.

10. The primary contaminants of concern, those for which there are remediation performance standards, are benzene, nickel, and toxaphene.

Performance Standards

11. This section should be revised to reflect the performance standards contained in the Consent Decree and Statement of Work. The inclusion of tables 2-4, which have been taken out of context from the RI/FS and the ROD, should be deleted or clarified.

Five-year Review Process

12. We question the extent to which reviewing the implementation of the remedy is relevant to the current conditions.

Data Review

13. ¶ 1- We believe that measurable attenuation of benzene has been achieved. We are unaware of any documentation that supports the notion that toxaphene is transported through colloidal processes, at this site or any other site. This sentence should be deleted.

14. ¶ 2- This paragraph discussing degradation of toxaphene is also not relevant to the five-year review, because there is no requirement to show degradation. Furthermore, it is impossible to establish toxaphene because toxaphene was not detected.

Site Inspection

15. It should be noted that an HDPE lined culvert was installed in the drainage ditch on the eastern boundary of the landfill. This was not required by EPA and was performed by Hercules at the request of the Glynn County School Board.

Interviews - Lavon Revells and Dr. Keith Maruya

16. Dr. Maruya was not involved at this site in any aspect of the site characterization, toxaphene analysis, or the solidification/stabilization remedy, nor any of the groundwater monitoring.

17. There is no difference between the "Task Force method" and the "standard EPA method". Refer to SW-846 8081A Section 7.6.1.3 " Quantitate Toxaphene using the total area of the Toxaphene pattern or using 4 to 6 major peak.

Technical Assessment

Question A - Is the remedy functioning as intended by the decision documents?

18. A statement evaluating the functionality and performance of the OU-2 remedy should be added.

19. EPA should outline the remedial action objectives and performance standards for the site. The redline strikeout version suggests an approach.

Question B - Are the exposure assumptions, toxicity data, cleanup levels and
~~remedial action objectives (RAOs) used at the time of the remedy~~
selection still valid?

20. EPA should address this question more directly. Hercules believes the toxicity and exposure assumptions, and risk management decisions to be extremely conservative. Hercules believes that EPA's slope factor is overly conservative and submitted the following document to EPA. "Toxaphene Basis for a Change and Recalculation of the Cancer Potency Factor", Hauswirth, Dr. J. H, Sielken, Dr. R.L. 1997.

Changes in Standards and To-Be-Considered (TBC) Criteria

21. It is our understanding that ARAR's are "fixed" at the Record of Decision and that a change in the promulgated standard does not automatically change the requirements of the remedy as could be interpreted in this report.

Technical Assessment Summary

22. ¶ 1 – We believe that is outside the scope of a five-year review process to recommend research into "possible effects of weathered toxaphene" in this report.

Issues

23. This section should be revised and an explanation should be provided here or somewhere else in the document that clearly defines the issue and supports the recommendations in Table 6.

24. Low Flow/Low Purge Sampling is not a biased method, but a more representative sampling method. According to EPA literature it is a " state of the science" practice for groundwater sampling and is also recognized in EPA Region IV's QA manual and in the past was on Region IV's Website. The scientific underpinning of this method is that the traditional sampling methods over-stress the well and are not representative of aquifer conditions. Refer to Attached Paper "Low-Flow (Minimal Drawdown) Ground-Water Sampling Procedures" Puls, R.W., Barcelona, M.J.

Recommendations and Follow-up Actions

25. This should be revised to follow pending outcome of the rewrite of "Issues" section. Specific comments are added in the red-line strikeout document.

Protectiveness Statement

26. Toxaphene has been non-detect in groundwater prior to and subsequent to the implementation of the Remedy. Measurable attenuation of benzene has been achieved. The performance standards have been satisfied and therefore we believe the protectiveness statement should be changed accordingly to reflect this. The following is suggested language. "The remedial actions at the site are protective of human health and the environment and ground-water performance standards have been proven". The section ~~"inappropriate sampling and analytical techniques" should be~~ deleted as it could imply that they were not used for past monitoring. The only remaining issue in groundwater is to demonstrate that benzene will eventually attenuate to below the MCL.

Next Review

27. With the exception of benzene in monitoring well # 5, groundwater objectives have been achieved.

Documents Reviewed

28. The Consent Decree and Statement of Work should be added to both citations for the ROD's. The ROD for OU-1 is not cited correctly.

29. A literature citation has been added to "The Application of Standard Methods....."

30. The O&M plan, the governing document for post construction remedial action activities, should be cited as a reference.

31. The relevance of these articles is vague and/or inaccurate and should be clarified and discussed if they are to remain in the report. A recent publication on the general subject of toxaphene/weathered toxaphene has been provided for consideration.

Conversation Outlines and Summaries

32. The bullets that do not specifically pertain to this site should be deleted.

Hopefully the aforementioned comments show our concerns with the Draft Five-Year Review Report the way it is currently written. We would be glad to meet with you to discuss these comments and as always I can be reached at (302) 995-3456 if you have any questions regarding this document.

Sincerely,

Timothy D. Hassett
Hercules Incorporated
Staff Environmental Engineer

TDH/ijc
009-5yrltr

cc: B.J. Hough Hercules/ 8139/16
R. L. Williams Hercules/
J. Riley – Hercules/Plaza/8256 SW
~~K.P. Wileman – Hercules/Brunswick~~
S. W. Webb - RMT

Attachments:

Redline/Strikeout version Draft Five-Year Review Report
GAO RCED-94-220 - Improved Reviews and Guidance Could Reduce Inconsistencies in Risk Assessments.

GAO TRCED-95-206 -Risk Assessment Assumptions and Issues
The Application of Standard Methods for the Determination of Toxaphene in Environmental Media, Francis J. Carlin, Jr., Lavon Revells, and Danny Reed, Chemosophere 41 (2000) 481-486.

"Toxicity And Tissue Selective Accumulation Of Sediment Weathered And Unmodified Toxaphene", Jeanne M. Zimmerman1 and Keith A. Maruya, Dioxin 2003

"Toxaphene Basis for a Change and Recalculation of the Cancer Potency Factor", Hauswirth, Dr. J. H, Sielken, Dr. R.L. 1997.

"Low-Flow (Minimal Drawdown) Ground-Water Sampling Procedures"
Robert W. Puls1 and Michael J. Barcelona2 EPA 1996

NATIONAL ARCHIVES AND RECORDS ADMINISTRATION 1985

Federal Register

Thursday,
February 21, 2008

Part II

Environmental Protection Agency

Drinking Water Contaminant Candidate List 3—Draft; Notice

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OW–2007–1189 FRL–8529–7]

RIN 2040–AD99

Drinking Water Contaminant Candidate List 3—Draft

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA is publishing for public review and comment a draft list of contaminants that are currently not subject to any proposed or promulgated national primary drinking water regulations, that are known or anticipated to occur in public water systems, and which may require regulations under the Safe Drinking Water Act (SDWA). This is the third Contaminant Candidate List (CCL 3) published by the Agency since the SDWA amendments of 1996.

This draft CCL 3 includes 93 chemicals or chemical groups and 11 microbiological contaminants. The EPA seeks comment on the draft CCL 3, the approach used to develop the list, and other specific contaminants.

DATES: Comments must be received on or before May 21, 2008.

ADDRESSES: Submit your comments, identified by Docket ID No. EPA–HQ–OW–2007–1189, by one of the following methods:

- *http://www.regulations.gov:* Follow the on-line instructions for submitting comments.
- *Mail:* Water Docket, Environmental Protection Agency, Mailcode: 2822T, 1200 Pennsylvania Ave., NW., Washington, DC 20460.
- *Hand Delivery:* Water Docket, EPA Docket Center (EPA/DC) EPA West, Room 3334, 1301 Constitution Ave., NW., Washington, DC. Such deliveries are only accepted during the Docket's normal hours of operation, and special arrangements should be made for deliveries of boxed information.

Instructions: Direct your comments to Docket ID No. EPA–HQ–OW–2007–1189. EPA's policy is that all comments received will be included in the public docket without change and may be made available online at *http://www.regulations.gov*, including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through *http://www.regulations.gov* or e-mail. The *http://www.regulations.gov* Web site is an "anonymous access" system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through *http://www.regulations.gov* your e-mail address will be automatically captured and included as part of the comment that is placed in the public docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD–ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses. For additional instructions on submitting comments, go to Unit I.B of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: All documents in the docket are listed in the *http://www.regulations.gov* index. Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other ~~material, such as copyrighted~~ material, will be publicly available only in hard copy. Publicly available docket materials are available either electronically in *http://www.regulations.gov* or in hard copy at the Water Docket, EPA/DC, EPA West, Room 3334, 1301 Constitution Ave., NW., Washington, DC. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the EPA Docket Center is (202) 566–2426.

FOR FURTHER INFORMATION CONTACT: For information on chemical contaminants contact Thomas Carpenter, Office of Ground Water and Drinking Water, Standards and Risk Management Division, at (202) 564–4885 or e-mail *carpenter.thomas@epa.gov*. For information on microbial contaminants contact Tracy Bone, Office of Ground Water and Drinking Water, at 202–564–5257 or e-mail *bone.tracy@epa.gov*. For general information contact the EPA Safe Drinking Water Hotline at (800) 426–4791 or e-mail: *hotline-sdwa@epa.gov*.

Abbreviations and Acronyms

<—less than
≤—less than or equal to
>—greater than
≥—greater than or equal to
µ—microgram, one-millionth of a gram
µg/L—micrograms per liter
ATSDR—Agency for Toxic Substances and Disease Registry
AWWA—American Water Works Association
CASRN—Chemical Abstract Services Registry Number
CDC—Centers for Disease Control and Prevention
CCL—Contaminant Candidate List
CCL 1—EPA's First Contaminant Candidate List
CCL 2—EPA's Second Contaminant Candidate List
CCL 3—EPA's Third Contaminant Candidate List
CFR—Code of Federal Regulations
CUS/IUR—Chemical Update System/Inventory Update Rule
DBP—disinfection byproduct
DWEL—drinking water equivalent level
EPA—United States Environmental Protection Agency
ESA—ethanesulfonic acid
FDA—United States Food and Drug Administration
FR—**Federal Register**
g—gram
HAAs—haloacetic acids
IOCs—inorganic contaminants
~~IRIS—Integrated Risk Information~~ System
kg—kilogram
L—liter
LD_{50}—lethal dose 50; an estimate of a single dose that is expected to cause the death of 50 percent of the exposed animals; it is derived from experimental data.
lbs—pounds
LOAEL—lowest-observed-adverse-effect level
MCL—maximum contaminant level
MCLG—maximum contaminant level goal
MRDD—maximum recommended daily dose
mg/kg—milligrams per kilogram body weight
mg/kg/day—milligrams per kilogram body weight per day
mg/L—milligrams per liter
MMWR—*Morbidity and Mortality Weekly Report*
NAS—National Academy of Sciences
NCI—National Cancer Institute
NCOD—National Contaminant Occurrence Database
NDWAC—National Drinking Water Advisory Council
NOAEL—no-observed-adverse-effect level

NRC—National Academy of Sciences' National Research Council
NPDWR—national primary drinking water regulation
NTP—National Toxicology Program
OPP—Office of Pesticide Programs
PFOA—perfluorooctanoic acid
PFOS—perfluorooctane sulfonic acid
PWS—public water system
RfD—reference dose
SAB—Science Advisory Board
SDWA—Safe Drinking Water Act
TCR—Total Coliform Rule
TD_{50}—tumorigenic dose 50; The dose-rate which if administered chronically for the standard life-span of the species will have a 50% probability of causing tumors at some point during that period.
TRI—Toxics Release Inventory
TDS—training data set
UCM—Unregulated Contaminant Monitoring
UCMR 1—First Unregulated Contaminant Monitoring Regulation
UCMR 2—Second Unregulated Contaminant Monitoring Regulation
US—United States of America
USDA—United States Department of Agriculture
USGS—United States Geological Survey
WBDO—waterborne disease outbreak
WHO—World Health Organization
yr—year

SUPPLEMENTARY INFORMATION:

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I. General Information

A. Does This Action Impose Any Requirements on My Public Water System?

The draft Contaminant Candidate List 3 (CCL 3) or the final CCL 3, when published, will not impose any requirements on anyone. Instead, this action notifies interested parties of the availability of EPA's draft CCL 3 and seeks comment on the contaminants listed.

B. What Should I Consider as I Prepare My Comments for EPA?

You may find the following suggestions helpful for preparing your comments:

- Explain your views as clearly as possible.
- Describe any assumptions that you used.
- Provide any technical information and/or data you used that support your views.
- Provide specific examples to illustrate your concerns.
- Offer alternatives.

Make sure to submit your comments by the comment period deadline. To ensure proper receipt by EPA, identify the appropriate docket identification number in the subject line on the first page of your response. It would also be helpful if you provided the name, date, and **Federal Register** citation related to your comments.

II. Purpose, Background, and Summary of This Action

This section briefly summarizes the purpose of this action, the statutory requirements, previous activities related to the Contaminant Candidate List (CCL), and the approach used to develop the CCL 3.

A. What Is the Purpose of This Action?

The Safe Drinking Water Act (SDWA), as amended in 1996, requires EPA to publish a list of currently unregulated contaminants that may pose risks for drinking water (referred to as the Contaminant Candidate List, or CCL) and to make determinations on whether to regulate at least five contaminants from the CCL with a national primary drinking water regulation (NPDWR) (section 1412(b)(1)). The 1996 SDWA requires the Agency to publish both the CCL and the regulatory determinations every five years. The purpose of this action is to present EPA's draft list of contaminants on the CCL 3, a description of the selection process, and the rationale used to make the list.

This action also includes a request for comment on the Agency's draft CCL 3, the approach used to develop the list, and other specific contaminants.

B. Background on the CCL, Regulatory Determinations, and Unregulated Contaminant Monitoring

1. Statutory Requirements for CCL and Regulatory Determinations

Section 1412(b) (1) of SDWA, as amended in 1996, requires EPA to publish the Contaminant Candidate List every five years. SDWA specifies that the list must include contaminants that are not subject to any proposed or promulgated NPDWRs, are known or anticipated to occur in public water systems (PWSs), and may require regulation under SDWA.

The 1996 SDWA Amendments also specify three criteria to determine whether a contaminant may require regulation:

- The contaminant may have an adverse effect on the health of persons;
- The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and
- In the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

In developing the draft CCL 3, the Agency considered the best available data and information for unregulated contaminants. As required under the Safe Drinking Water Act, EPA evaluated substances identified in section 101(14) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 and substances registered as pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act. In addition to these required data sources, the Agency also developed the National Contaminant Occurrence Database (NCOD) established under section 1445(g) of SDWA. Substances from NCOD were included in the initial set of contaminants considered for the draft CCL 3.

SDWA also directs the Agency to consider the health effects and occurrence information for unregulated contaminants to identify those contaminants that present the greatest public health concern related to exposure from drinking water. In selecting contaminants for the draft CCL 3, adverse health effects that may pose a greater risk to subgroups which represent a meaningful portion of the population were considered. Adverse health effects associated with infants, children, pregnant women, the elderly, and individuals with a history of serious illness were evaluated for both chemicals and microbes. The specific analyses and evaluations used by the Agency are discussed and cited in the relevant sections of this notice.

2. The First Contaminant Candidate List

Following the 1996 SDWA Amendments, EPA sought input from the National Drinking Water Advisory Council (NDWAC) on the process that should be used to identify contaminants for inclusion on the first CCL (CCL 1). For chemical contaminants, the Agency developed screening and evaluation criteria based on the recommendations provided by NDWAC. For microbiological contaminants, NDWAC recommended that the Agency seek external expertise to identify and select potential waterborne pathogens. As a result, an external group of microbiologists and public health experts developed the criteria for screening, conducted an evaluation of microbial agents, and selected the initial list of microbiological contaminants for the CCL 1.

The draft CCL 1 was published on October 6, 1997 (62 *FR* 52193 (USEPA, 1997)). After consideration of all comments, EPA published the final CCL 1, which included 50 chemical and 10 microbiological contaminants, on March 2, 1998 (63 *FR* 10273 (USEPA, 1998 b)). A more detailed discussion of how EPA developed CCL 1 can be found in the 1997 and the 1998 **Federal Register** notices (62 *FR* 52193 (USEPA, 1997) and 63 *FR* 10273 (USEPA, 1998 b)).

3. The Regulatory Determinations for CCL 1

EPA published its preliminary regulatory determinations for a subset of contaminants listed on CCL 1 on June 3, 2002 (67 *FR* 38222 (USEPA, 2002 b)). The Agency published its final regulatory determinations on July 18, 2003 (68 *FR* 42898 (USEPA, 2003 a)). EPA identified 9 contaminants from the 60 contaminants listed on CCL 1 that had sufficient data and information available to make regulatory determinations. The 9 contaminants were *Acanthamoeba*, aldrin, dieldrin, hexachlorobutadiene, manganese, metribuzin, naphthalene, sodium, and sulfate. The Agency determined that a national primary drinking water regulation was not necessary for any of these 9 contaminants. The Agency issued guidance on *Acanthamoeba* and health advisories for magnesium, sodium, and sulfate.

4. The Second Contaminant Candidate List

The Agency published its draft second CCL (CCL 2) **Federal Register** notice on April 2, 2004 (69 *FR* 17406 (USEPA, 2004)) and the final CCL 2 **Federal Register** notice on February 24, 2005 (70 *FR* 9071 (USEPA, 2005 b)). The CCL 2 carried forward the 51 remaining chemical and microbial contaminants that were listed on CCL 1.

5. The Regulatory Determinations for CCL 2

EPA published its preliminary regulatory determinations for a subset of contaminants listed on CCL 2 on May 1, 2007 (72 *FR* 24015 (USEPA, 2007 d)). EPA identified 11 contaminants from the 51 contaminants listed on CCL 2 that had sufficient data and information available to make preliminary regulatory determinations. The 11 contaminants are boron, the dacthal mono- and di-acid degradates, 1,1-dichloro-2,2-bis (p-chlorophenyl) ethylene (DDE), 1,3-dichloropropene, 2,4-dinitrotoluene, 2,6-dinitrotoluene, s-ethyl propylthiocarbamate (EPTC), fonofos, terbacil, and 1,1,2,2-tetrachloroethane. The Agency has made a preliminary determination that a national primary drinking water regulation is not necessary for any of these 11 contaminants. The Agency is scheduled to publish its final regulatory determinations in 2008. In the May 1, 2007 *FR* notice, the Agency indicated that additional information was needed to make the regulatory determinations for perchlorate and methyl tertiary butyl ether (MTBE) and provided a summary of the current health effects, occurrence, and exposure information.

6. The Unregulated Contaminant Monitoring Rule

SDWA provides EPA with the authority to require all large and a subset of small systems to monitor for unregulated contaminants. EPA may require monitoring for up to 30 contaminants under the Unregulated Contaminant Monitoring Rule (UCMR). Since the 1996 SDWA amendments, the Agency has issued two UCMRs (UCMR 1 and UCMR 2). UCMR 1 was promulgated on September 17, 1999 (64 *FR* 50556 (USEPA, 1999)) and UCMR 2 on January 4, 2007 (72 *FR* 367 (USEPA, 2007 a)), followed by two revisions published later in January 2007 (72 *FR* 3916 (USEPA, 2007 b) and 72 *FR* 4328 (USEPA, 2007 c)). Monitoring under UCMR 2 will take place during the 2008–2010 time period.

UCMR 2 requires monitoring for several pesticides and pesticide degradates, five polybrominated diphenyl ether (PBDE) flame retardants, a group of nitrosamines and two munitions (TNT and RDX). All of the chemicals on UCMR 2 were included among the contaminants evaluated for CCL 3. Data collected under the UCMR are an important source of occurrence information for the CCL process.

7. The Third Contaminant Candidate List

In 1998, the Agency sought advice from the National Academy of Sciences' National Research Council (NRC) on how to improve the CCL process. The NRC published its recommendations on the CCL process in 2001 (NRC, 2001). The NRC proposed a broader, more reproducible process to identify the CCL than the process used by EPA in the first CCL. The NRC recommended that EPA develop and use a multi-step process for creating CCL 3 and future CCLs, whereby a broadly defined "universe" of potential drinking water contaminants is identified, assessed, and reduced to a preliminary CCL (PCCL) using simple screening criteria. All of the contaminants on the PCCL would then be assessed in more detail using a classification tool to evaluate the likelihood that specific contaminants could occur in drinking water at levels and at frequencies that pose a public health concern.

In 2002, the Agency sought input from the National Drinking Water Advisory Council (NDWAC) on how to implement the NRC's recommendations to improve the CCL process. NDWAC agreed that EPA should proceed with the NRC's recommendations and provided some additional considerations, including the overarching principles the Agency should follow. The NDWAC workgroup met 10 times between September 2002 and May 2004. The NDWAC issued its recommendations in "The National Drinking Water Advisory Council Report on the CCL Classification Process to the U.S. Environmental Protection Agency" (NDWAC, 2004).

NDWAC recommended two guiding principles for construction of the CCL universe, which are:

- The universe should include those contaminants that have demonstrated or have potential occurrence in drinking water, and
- The universe should include those contaminants that have demonstrated or have potential adverse health effects.

These inclusionary principles apply to the selection of contaminants for initial CCL consideration.

The NDWAC also recommended that the universe of contaminants should be screened based on widely available data elements that indicate important health effects and occurrence information. This screening step should be as simple as possible and capable of identifying contaminants of the greatest significance for further consideration. Consideration of a classification approach was also recommended to increase the transparency and reproducibility of the CCL decision process. NDWAC recommended that EPA pursue classification models that build on the screening criteria to further characterize the adverse health effects and occurrence of chemical contaminants. NDWAC noted that the classification models are tools to help prioritize contaminants for the CCL. The model results, available information used by the model, and expert reviews should be ~~used to determine which contaminants~~ are listed for the next CCL. The process to develop the models should be viewed as iterative, and EPA should involve experts and allow opportunities for meaningful public comment on the evaluation of contaminants.

NDWAC recommended several overarching principles that EPA should use to develop the CCL. In addition to the need for transparency and public participation, these overarching recommendations include:

- Integrate expert judgment throughout the CCL process. Expert judgment is inherent throughout the development of the CCL process and in implementing that process once it is developed. Critical reviews, involving various types of expert consultation and collaboration, will be useful at key points in the new, evolving CCL process.
- Conduct an active surveillance and nomination/evaluation processes to ensure timely identification of information relevant to new and emerging agents.
- Apply an adaptive management approach (i.e., an approach that can be refined in future iterations as more knowledge is acquired) to implement the CCL process. The development of any model should be an adaptive process, and should be reviewed by experts with consideration given to updating the process with each successive CCL cycle.

NDWAC also recognized that there were significant differences in the methods and information used to characterize chemical and microbiological contaminants. Chemical contaminants tend to be characterized by toxicological and occurrence data that can be modeled or estimated if measurement is not possible. These discrete characteristics are often captured in data sources. For microbes, the adverse health effects from exposure are characterized by clinical or epidemiological data and there are few methods to estimate or model their occurrence. Limited sources of tabular data for microbes may require evaluation of primary literature, technical reports, monographs, and reference books to identify a universe of microbes for consideration. NDWAC recommended the Agency use human pathogens as the starting point for identifying microorganisms considered for inclusion in the CCL and apply a ~~two-step evaluation of those pathogens~~.

C. Summary of the Approach Used To Identify and Evaluate Candidates for CCL 3

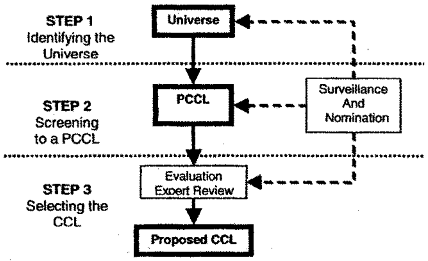
The Agency revised the CCL process used in previous efforts based on the knowledge and experience it has gained from evaluating unregulated contaminants and the recommendations and advice from NRC and NDWAC. Based on these recommendations the Agency developed and implemented a classification approach that identifies priority drinking water contaminants in a transparent and reproducible manner that is amenable to an adaptive management approach.

The Agency's approach to classifying contaminants is based on available data to characterize the occurrence and adverse health risks a contaminant may pose to consumers of public water systems. EPA developed and implemented the following multi-step CCL process to identify contaminants for inclusion on the Draft CCL 3.

- Identify a broad universe of potential drinking water contaminants (called the CCL 3 Universe). EPA evaluated 284 data sources that may identify potential chemical and microbial contaminants and selected a set of approximately 7,500 chemical and microbial contaminants from these data sources for initial consideration.
- Apply screening criteria to the CCL 3 Universe to identify those contaminants that should be further evaluated. Contaminants not passing the screening criteria remained in the universe. The screening criteria EPA developed are based on a contaminant's potential to occur in public water systems and the potential for public health concern. Applying these criteria narrows the universe of contaminants to a Preliminary-CCL (or PCCL).
- Identify contaminants from the PCCL to include on the CCL based on a more detailed evaluation of occurrence and health effects. For chemicals, EPA used structured classification models as tools to evaluate and identify drinking water priority contaminants. Decisions to include chemicals were made using the model results and the best available data to identify contaminants that may occur in PWSs and may cause adverse health effects. EPA used a decision tree approach for microbial contaminants to ~~identify those contaminants that have~~ the potential to occur in PWSs and transmit waterborne disease. These two approaches resulted in a draft list of chemicals and microbes for inclusion on the Draft CCL 3.
- Incorporate public input and expert review in the CCL process. EPA sought public input by asking for nominations of contaminants to consider for the CCL (71 *FR* 60704 (USEPA, 2006 b)) and incorporated these nominations in the three key steps already discussed. EPA also convened several expert panels for both chemicals and microbes to review, and provide input and comment, on the CCL 3 process and on a review of a preliminary draft CCL 3.

Exhibit 1 illustrates the CCL multi-step approach that resulted from the Agency's efforts, input, and collaboration with NRC and NDWAC. This generalized process is applied to both chemical and microbial contaminants, though the specific execution of particular steps differs in detail.

Exhibit 1. Schematic of CCL classification process



EPA provides a more detailed discussion of the analyses and decisions it made to develop the Draft CCL 3 in the EPA Water Docket. EPA prepared several support documents that are available for review at *http://www.regulations.gov*. These documents include:

- Three comprehensive support documents for the chemicals entitled, "Contaminant Candidate List 3 Chemicals: Identifying the Universe" (USEPA, 2008 a), "Contaminant Candidate List 3 Chemicals: Screening to a PCCL" (USEPA, 2008 b), and "Contaminant Candidate List 3 Chemicals: Classification of the PCCL to the CCL" (USEPA, 2008 c). These documents describe in detail how the classification process was developed and used to select the chemicals for the Draft CCL.
- Three comprehensive support documents for the microbes entitled, "Contaminant Candidate List 3 Microbes: Identifying the Universe" (USEPA, 2008 d), "Contaminant Candidate List 3 Microbes: Screening to the PCCL" (USEPA, 2008 e), and "Contaminant Candidate List 3 Microbes: PCCL to CCL Process" (USEPA, 2008 f). These documents describe the microbial listing process in detail.
- The Agency also prepared summaries of stakeholder involvement and reviews conducted on the CCL process and draft list. These documents are also available in the EPA Water Docket and at *http://www.regulations.gov*.
- National Drinking Water Advisory Council Report on the CCL Classification Process to the U.S. Environmental Protection Agency, May 19, 2004.
- A nominations and surveillance report, entitled "Summary of the Nominations for the Third Contaminant Candidate List" (USEPA, 2008 g), which describes the nominations process and the contaminants that were nominated as part of EPA's process.
- Two documents summarizing the expert review of the chemical and microbial processes, entitled "Chemical Expert Input and Review for the Third Contaminant Candidate List" (USEPA, 2008 h) and "Microbial Expert Input and Review for the Third Contaminant Candidate List" (USEPA, 2008 i).

D. What Is on EPA's Draft CCL 3?

EXHIBIT 2.—DRAFT CONTAMINANT CANDIDATE LIST 3: MICROBIAL CONTAMINANTS

Pathogens
Caliciviruses
Campylobacter jejuni
Entamoeba histolytica
Escherichia coli (0157)
Helicobacter pylori
Hepatitis A virus
Legionella pneumophila
Naegleria fowleri
Salmonella enterica
Shigella sonnei
Vibrio cholerae

CHEMICAL CONTAMINANTS

Common name—registry name	CASRN
alpha-Hexachlorocyclohexane	319–84–6
1,1,1,2-Tetrachloroethane	630–20–6
1,1-Dichloroethane	75–34–3
1,2,3-Trichloropropane	96–18–4
1,3-Butadiene	106–99–0
1,3-Dinitrobenzene	99–65–0
1,4-Dioxane	123–91–1
1-Butanol	71–36–3
2-Methoxyethanol	109–86–4
2-Propen-1-ol	107–18–6
3-Hydroxycarbofuran	16655–82–6
4,4'-Methylenedianiline	101–77–9
Acephate	30560–19–1
Acetaldehyde	75–07–0
Acetamide	60–35–5
Acetochlor	34256–82–1
Acetochlor ethanesulfonic acid (ESA)	187022–11–3
Acetochlor oxanilic acid (OA)	184992–44–4
Acrolein	107–02–8
Alachlor ethanesulfonic acid (ESA)	142363–53–9
Alachlor oxanilic acid (OA)	171262–17–2
Aniline	62–53–3
Bensulide	741–58–2
Benzyl chloride	100–44–7
Butylated hydroxyanisole	25013–16–5
Captan	133–06–2
Chloromethane (Methyl chloride)	74–87–3
Clethodim	110429–62–4
Cobalt	7440–48–4
Cumene hydroperoxide	80–15–9
Cyanotoxins (3).	
Dicrotophos	141–66–2
Dimethipin	55290–64–7
Dimethoate	60–51–5
Disulfoton	298–04–4
Diuron	330–54–1
Ethion	563–12–2
Ethoprop	13194–48–4
Ethylene glycol	107–21–1
Ethylene oxide	75–21–8
Ethylene thiourea	96–45–7
Fenamiphos	22224–92–6
Formaldehyde	50–00–0
Germanium	7440–56–4
HCFC–22	75–45–6
Hexane	110–54–3
Hydrazine	302–01–2
Methamidophos	10265–92–6
Methanol	67–56–1
Methyl bromide (Bromomethane)	74–83–9
Methyl tert-butyl ether	1634–04–4

CHEMICAL CONTAMINANTS—Continued

Common name—registry name	CASRN
Metolachlor	51218–45–2
Metolachlor ethanesulfonic acid (ESA)	171118–09–5
Metolachlor oxanilic acid (OA)	152019–73–3
Molinate	2212–67–1
Molybdenum	7439–98–7
Nitrobenzene	98–95–3
Nitrofen	1836–75–5
Nitroglycerin	55–63–0
N-Methyl-2-pyrrolidone	872–50–4
N-nitrosodiethylamine (NDEA)	55–18–5
N-nitrosodimethylamine (NDMA)	62–75–9
N-nitroso-di-n-propylamine (NDPA)	621–64–7
N-Nitrosodiphenylamine	86–30–6
N-nitrosopyrrolidine (NPYR)	930–55–2
n-Propylbenzene	103–65–1
o-Toluidine	95–53–4
Oxirane, methyl-	75–56–9
Oxydemeton-methyl	301–12–2
Oxyfluorfen	42874–03–3
Perchlorate	14797–73–0
Permethrin	52645–53–1
PFOA (perfluorooctanoic acid)	335–67–1
Profenofos	41198–08–7
Quinoline	91–22–5
RDX (Hexahydro–1,3,5–trinitro–1,3,5–triazine)	121–82–4
sec-Butylbenzene	135–98–8
Strontium	7440–24–6
Tebuconazole	107534–96–3
Tebufenozide	112410–23–8
Tellurium	13494–80–9
Terbufos	13071–79–9
Terbufos sulfone	56070–16–7
Thiodicarb	59669–26–0
Thiophanate-methyl	23564–05–8
Toluene diisocyanate	26471–62–5
Tribufos	78–48–8
Triethylamine	121–44–8
Triphenyltin hydroxide (TPTH)	76–87–9
Urethane	51–79–6
Vanadium	7440–62–2
Vinclozolin	50471–44–8
Ziram	137–30–4

III. What Analyses Did EPA Use To Develop the Draft CCL 3?

A. Classification Approach for Chemicals

1. Identifying the Universe

In the first step in the approach, EPA compiled potential data sources, including sources identified at a stakeholder workshop sponsored by the American Water Works Association (AWWA), to develop a broad universe of potential drinking water contaminants, as shown in Exhibit 1. This compilation identified the 284 data sources that were assessed for the CCL Universe.

EPA developed a decision tree for data source selection that was based on four assessment factors, which were applied to all of the potential data sources:

- Relevance. Ensures that the data source provided information on demonstrated or potential health effects, occurrence, or potential occurrence using surrogate information (e.g., environmental release, environmental fate, and transport properties);
- Completeness. Ensures that the data source had minimum record requirements—contact name, description of the data elements, and how the data were obtained;
- Redundancy. Ensures that the data source does not contain information identical to other more comprehensive data sources; and
- Retrievability. Ensures that the data in the source are formatted for automated retrieval. Each source was accessed on-line (or as provided by the source) and reviewed.

Basic information about the source, its purpose, and the data elements it contained, was compiled and documented. Every source was evaluated using all assessment factors sequentially. Those sources that met all four factors became the prime sources that formed the "Universe of Data Sources." Sources that passed the first three factors, but were not retrievable, were designated as supplemental data sources, to be consulted as necessary (e.g., to fill in data gaps) in the development of the CCL. Some of the sources that were not easily retrievable were identified as "unique" or "exceptional" because of the importance of their data (i.e., the Hazardous Substance Database). EPA included chemicals from these sources in the Universe.

After application of the four assessment factors, 39 sources (Exhibit 3) met all four factors or were considered as exceptional. These sources were the primary sources used to develop the CCL Chemical Universe. The details of the how EPA compiled the list of data sources is discussed in the document entitled, "CCL 3 Chemicals: Identifying the Universe" (USEPA, 2008 a).

EXHIBIT 3.—SOURCES THAT COMPRISE THE CHEMICAL UNIVERSE OF DATA SOURCES FOR THE CCL PROCESS

Name of data source
1. ATSDR CERCLA Priority List.
2. ATSDR Minimal Risk Levels (MRLs).
3. Chemical Toxicity Database—Ministry of Health and Welfare, Japan.
4. Chemical Update System/Inventory Update Rule (CUS/IUR)—EPA.
5. Cumulative Estimated Daily Intake/Acceptable Daily Intake (CEDI/ADI) Database—FDA.
6. Database of Sources of Environmental Releases of Dioxin-Like Compounds in the United States—EPA.
7. Distributed Structure Searchable Toxicity Public Database Network (DSSTox)—EPA.
8. Everything Added to Food in the United States (EAFUS) Database—FDA.
9. Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) List—EPA.
10. Generally Regarded As Safe (GRAS) Substance List—FDA.
11. Guidelines for Canadian Drinking Water Quality (CADW): Summary of Guidelines—Health Canada.
12. Hazardous Substances Data Bank (HSDB)—NLM.
13. Health Advisories (HA) Summary Tables—EPA.
14. High Production Volume (HPV) Chemical List—EPA.
15. Indirect Additives Database—FDA.
16. Integrated Risk Information System (IRIS)—EPA.
17. International Agency for Research on Cancer (IARC) Monographs.
18. International Toxicity Estimates for Risk (ITER) Database—TERA.
19. Joint Meeting On Pesticide Residues (JMPR)—2001 Inventory of Pesticide Evaluations—WHO, FAO.
20. National Drinking Water Contaminant Occurrence Database (NCOD)—Round 1&2—EPA.
21. National Drinking Water Contaminant Occurrence Database (NCOD)—Unregulated Contaminant Monitoring Rule (UCMR)—EPA.
22. National Inorganics and Radionuclides Survey (NIRS)—EPA.
23. National Pesticide Use Database—NCFAP.

EXHIBIT 3.—SOURCES THAT COMPRISE THE CHEMICAL UNIVERSE OF DATA SOURCES FOR THE CCL PROCESS—Continued

Name of data source
24. National Reconnaissance of Emerging Contaminants (NREC)—USGS Toxic Substances Hydrology Program.
25. National Toxicology Program (NTP) Studies.
26. National Water Quality Assessment (NAWQA)—USGS.
27. OSHA 1988 Permissible Exposure Limits (PELs)—NIOSH.
28. Pesticide Data Program—USDA.
29. Pesticides Pilot Monitoring Program—USGS/EPA.
30. Risk Assessment Information System (RAIS)—Department of Energy—Chemical Factors.
31. Risk Assessment Information System (RAIS)—Department of Energy—Health Effects Data.
32. State of California Chemicals Known to the State to Cause Cancer or Reproductive Toxicity.
33. Substances Registry System (SRS)—EPA.
34. Syracuse Research Corporation (SRC)—BIODEG.
35. The Toxics Release Inventory (TRI)—EPA.
36. Toxic Substances Control Act (TSCA) List—EPA.
37. Toxicity Criteria Database—California Office of Environmental Health Hazard Assessment (OEHHA).
38. University of Maryland—Partial List of Acute Toxins/Partial List of Teratogens.
39. WHO Guidelines for Drinking Water Quality: Summary Tables.

There were approximately 26,000 unique substances identified from the 39 data sources. Because of the large number of unique substances identified, EPA developed an initial universe selection process. In the first phase of the data evaluation process, EPA identified the chemicals that were present in both health effects and occurrence data sources. The Agency queried the data sources and found that approximately 7,300 chemicals, or about one-third of the chemicals, were present in both health effects and occurrence data sources. Occurrence was defined broadly to include production data and environmental occurrence data. EPA placed these chemicals in the chemical universe to be further evaluated for screening to the PCCL. EPA then examined the rest of the approximately 18,600 chemicals left in the initial universe more closely to determine whether they were found only in health effects data sources or only in occurrence data sources. EPA found that approximately 5,100 chemicals were in health effects data sources only. Many of these chemicals were biochemical compounds (e.g., amino acids, sugars, steroids); mixtures and natural products (e.g., coal tar, petroleum related substances, rocks, stone, wool); and other entries that were identified as unique "substances" in the data sources but were not chemicals (e.g., turbidity, boot and shoe manufacture, surgical implants). EPA evaluated these to identify which ones are chemicals of greatest toxicological concern. Many of the chemicals fell into the category of greatest toxicological concern due to their classification as carcinogens. This is described in the report entitled, "CCL 3 Chemicals: Screening to a PCCL" (USEPA, 2008 b). Through this process, a total of 122 chemicals with only toxicity data were added to the 7,300 chemicals already in the CCL Chemical Universe.

The chemicals found only in occurrence sources were also categorized. The approximately 13,500 chemicals with only occurrence data were a diverse group, comprised of many different types of chemicals. Data sources that provide the amount of an individual chemical that is manufactured and produced account for 70 percent (or 9,344) of the total. The remaining 30 percent of chemicals are ~~from various other data sources~~ (i.e., finished water, ambient water, environmental release, environmental fate and transport properties, and food additives). EPA grouped these chemicals by the type of occurrence data for further evaluation. These included the following groupings:

- Chemicals with Finished or Ambient Water Data
- Chemicals with Release Data
- Chemicals with High Production Volumes

EPA added 42 chemicals with finished or ambient water data to the Universe despite the lack of health effects information in the data sources because of their demonstrated occurrence in ambient or potable water. In addition, disinfection byproducts and water treatment additives were added to the Chemical Universe. While there may not have been measured occurrence data for these chemicals in the universe of data sources, they are considered to have "default" occurrence data because they are formed in, or intentionally added to, drinking water supplies.

EPA also added 36 chemicals with an environmental release data source (e.g., those on the Toxics Release Inventory or with pesticide application data) to the Chemical Universe even though they lacked health effects data.

The largest group of chemicals found only in occurrence data sources had only production information. These contaminants include: organometallics, elements, salts of the inorganic elements, salts of organic acids, natural product organics (including oils, fatty acids, sugars, intermediary metabolites), and mixtures (e.g., petroleum related compounds, hydrocarbons, and others). Over half of the production chemicals are compounds and/or complexes of ~~elemental constituents; for example,~~ there were about 750 sodium or potassium salt compounds alone. In these cases, health effects data are not available for the exact compound, but are generally available for other related compounds or the key ion or elemental constituent (e.g., sodium). Nearly all elements found in inorganic or organic salts are represented in the Universe by other compounds with both health effects and occurrence data. EPA found only 10 elements (excluding carbon, hydrogen, and oxygen, and the inert gasses krypton, neon, and xenon) that did not otherwise have representative compounds with health effects data in the Universe. EPA added these compounds (i.e., europium, gadolinium, gold, lanthanum, praseodymium, platinum, polonium, samarium, terbium, and yttrium) to the Universe. After evaluation of the characteristics of the chemicals with production data and the amounts produced on a yearly basis, and because the primary constituents (i.e., elements) of the chemicals were already in the Chemical Universe, EPA decided to move only those produced at greater than 1 billion pounds per year to the CCL Chemical Universe when they lacked health effects information.

EPA added a total of 269 chemicals with only occurrence data to the CCL 3 Chemical Universe. The rest of the substances included in the original data sources were not included in the Universe.

The initial selection process brought into the CCL Chemical Universe all substances from the data sources that met the defined selection criteria, described above. Upon further review, EPA found the Chemical Universe also contained regulated as well as unregulated compounds, mixtures, and some substances that were not really chemicals. To further refine the initial list, EPA removed chemicals with a national primary drinking water regulation. These contaminants are already regulated; thus, their inclusion in the CCL process is unnecessary and does not meet the statutory requirement for selection of the CCL. EPA removed 1,006 chemicals, which is more than the number of primary drinking water standards. This is because regulated contaminants can be found in many forms and because many contaminants are regulated as part of a class or group(s). For example, EPA removed approximately 780 radionuclides from the initial list, because they are regulated as alpha and beta emitters. Also removed were various salts of regulated elements, and entries for ~~individual trihalomethanes, haloacetic~~ acids, polychlorinated biphenyls and polyaromatic hydrocarbons that are regulated as a group. The Agency has determined that it is inappropriate to include aldicarbs (aldicarb, aldicarb sulfoxide, and aldicarb sulfone) and nickel on the CCL. These contaminants are subject to regulation under SDWA section 1412(b)(2) and thus are not part of the contaminant selection process specified under SDWA section 1412(b)(1). In response to an administrative petition from the manufacturer Rhone-Poulenc, the Agency issued an administrative stay of the effective date of the maximum contaminant levels (MCLs) for aldicarbs, and they never became effective. NPDWRs for nickel were promulgated on July 17, 1992 (57 *FR* 31776 (USEPA, 1992)), but the MCL was later vacated and remanded by the D.C. Court of Appeals in response to a joint motion by EPA and industry parties challenging the nickel MCL and MCLG. Because these contaminants are subject to separate regulatory consideration, EPA has not included them in the CCL process.

EPA also removed substances that are considered a mixture of chemicals. EPA defines a mixture in this case as a combination of two or more chemicals/items that are not defined as a unique substance. Examples of substances in this category include "chlorinated compounds, aliphatic alcohols with more than 14 carbon atoms (c>14), coal-tar-containing shampoo, petroleum-related substances, resin acids, and rosin acids." Undefined mixtures, such as "diesel engine exhaust" were also included in this group.

EPA also removed "non-chemically defined" entries from further consideration for the initial list. Examples include: "solar radiation, wood dust, surgical implants, and welding fumes." Some of these substances are present in the data sources because they have been evaluated for their potential to cause cancer.

The final step removed biological agents from the initial list. Contaminants in this category are biological organisms that are being evaluated as part of the CCL 3 Microbiological Universe. Entries for biological entities were uploaded from the universe of data sources from various health effects data sources and pesticide data sources. Many biological entities were also removed as non-chemically defined.

During this phase of the data evaluation, 1,717 chemicals or substances were removed from the initial Chemical Universe, leaving approximately 6,000 chemicals that were designated as the CCL 3 Universe. A list of the CCL Chemical Universe is provided in the docket. EPA further evaluated these 6,000 chemicals in the next key step of the process.

2. Screening from the Universe to a PCCL

The next step in the CCL selection approach involved narrowing the Universe of chemicals to a PCCL, as shown in Exhibit 1. EPA considered and built upon NDWAC recommendations that the screening process be based on a contaminant's potential to occur in public water systems and the potential for public health concern, to select those contaminants that should move to the PCCL for further evaluation. The screening approach:

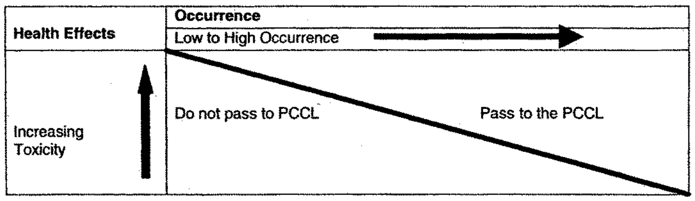
- Identifies chemicals that have relatively high toxicity with high potential to occur in PWSs;
- Identifies chemicals that have relatively high toxicity with minimal actual or potential occurrence in drinking water;
- Identifies chemicals that have high potential to occur in PWSs with relatively moderate toxicity; and
- Considers and uses as many of the available types of health effects and occurrence data identified in the data source evaluations as practical.

EPA compared the chemicals' health effects relative to their occurrence and developed analyses that specifically incorporate many types of available data into the screening criteria. The health effects information included quantitative, descriptive, or categorical information. Within each of these broad types of health effects information, there are multiple types of reported health related values from multiple sources. The health effects analyses conducted by EPA identified approaches to compare each of these data types and identified similarities among chemicals that could be used to define toxicity categories. The occurrence information also included many types of available data representative of a chemical's potential to occur in water. Occurrence data ranged from quantified detection in PWSs, to environmental release, to production data.

The basic framework EPA used in screening is shown in Exhibit 4. EPA categorized the CCL Chemical Universe ~~contaminants by their toxicity~~ along the vertical axis and by their occurrence on the horizontal axis. This allows for separation of chemicals into those that move to the PCCL based on their toxicity and occurrence properties (e.g., upper right in Exhibit 4) and those that are not further evaluated and remain in the CCL Chemical Universe (e.g., lower left in Exhibit 4).

EPA used a set of test chemicals to develop the screening criteria. This set of chemicals included regulated and unregulated chemicals that provided comprehensive information on health effects and occurrence in finished and/or ambient water as well as environmental release and production volume. EPA then used these criteria to select chemicals for the PCCL for further consideration. The following sections summarize how EPA developed the screening criteria by evaluating the available data for chemicals in the Universe, using the framework (Exhibit 4) and the test chemicals. A more detailed discussion is provided in the support document entitled, "CCL 3 Chemicals: Screening to a PCCL" (USEPA, 2008 b).

Exhibit 4: Partition for Screening the Universe



a. Health Effects Data Elements

EPA evaluated the toxicity information and health effects data compiled from the data sources in the Universe and these data varied greatly. Some of these data are quantitative (e.g., RfD, LOAEL, NOAEL, LD_{50}) and some are descriptive (e.g., cancer classifications or predictions). EPA designed the screening process to accommodate both types of health effects data.

The quantitative toxicity elements and values available in the Universe included the following:

- RfDs and equivalent (RfD-eq): RfDs, Minimum Risk Levels (MRLs) from ATSDR, Tolerable Daily Intakes (TDIs) from the World Health Organization (WHO), and Public Health Goals (PHGs) from California EPA. A reference dose is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. There are slight differences among Agencies in the methodologies used for some of the RfD equivalents.
- NOAELs—No Observed Adverse Effect Levels. The NOAEL is the highest dose evaluated in a study or group of studies that does not have a biologically significant adverse effect on the species evaluated as compared to controls.
- LOAELS—Lowest Observed Adverse Effect Levels. The LOAEL is the lowest dose evaluated in a study or group of studies that has a biologically significant adverse effect on the species evaluated as compared to the controls.
- TD_{50}s—Tumorigenic dose 50. The dose-rate which if administered chronically for the standard life-span of the species will have a 50 percent probability of causing tumors at some point during that period.
- MRDD—Maximum Recommended Daily Dose. Recommendations for the maximum adult daily therapeutic doses for pharmaceuticals.
- LD_{50}s—Lethal dose 50; an estimate of a single dose that is expected to cause the death of 50 percent of the exposed animals; it is derived from experimental data.

EPA used descriptive cancer data to group data elements into toxicity categories that provide gradation based upon the strength of the data. Sources for the descriptive cancer data included:

- U.S. EPA Cancer Groupings.
- IARC Cancer Groupings.
- NTP weight-of-evidence findings from cancer bioassays.
- National Cancer Institute (NCI) weight-of-evidence findings from cancer bioassays.
- EPA Water Disinfection By-Products with Carcinogenicity Estimates (DBP-CAN) groupings based on carcinogenic potential derived from Quantitative Structure Activity Relationship (QSAR) projections.

EPA divided the chemicals in the Universe into five toxicity categories for screening based upon the distribution of the toxicity value for each type of quantitative data element and/or the qualitative information on cancer weight-of evidence. The five toxicity categories are designated 1 through 5, with Toxicity Category 1 containing chemicals in the most toxic grouping and Toxicity Category 5 the least toxic grouping.

Based upon the distribution of the chemicals for each quantitative data element, EPA selected ranges of toxicity values for each toxicity category that differed based upon the type of data element. For example, the range of toxicity values that place a LOAEL in Toxicity Category 1 differs from the values used for a LD_{50}. Exhibit 5 displays the ranges for each data element and their respective Toxicity Categories.

Additional information which describes how EPA performed the analyses to select the toxicity categories is described in the document entitled, "CCL 3 Chemicals: Screening to a PCCL" (USEPA, 2008 b).

EXHIBIT 5.—POTENCY MEASURES FOR UNIVERSE DATA ELEMENTS PARTITIONED BASED ON TOXICITY

[mg/kg/day or mg/kg]

	RfD	NOAEL	LOAEL	MRDD	LD_{50}
Toxicity Category 1	<0.0001	<0.01	<0.01	<0.01	<1
Toxicity Category 2	0.0001–<0.001	0.01–<1	0.01–<1	0.01–<1	1–<50
Toxicity Category 3	0.001–<0.05	1–<10	1–<10	1–<10	50–<500
Toxicity Category 4	0.05–<0.1	10–<1000	10–<1000	10–<1000	500–5000
Toxicity Category 5	>0.1	>1000	>1000	>1000	>5000

EPA partitioned the cancer-related data elements in the Universe into the Toxicity Categories as shown in Exhibit 6. The cancer data placed chemicals in only the three highest Toxicity Categories. EPA did not use quantitative measures of dose-response for carcinogenicity in the screening criteria because more chemicals have categorical data and can be analyzed using this descriptive data than by cancer slope factors. In addition, EPA did not use descriptors indicating lack of carcinogenic potential or insufficient data to determine carcinogenic potential in categorizing chemicals because those descriptors apply only to the cancer endpoint and do not consider noncancer effects associated with exposure to the chemical.

EXHIBIT 6.—PARTITIONING OF CANCER DATA BASED ON TD_{50} VALUES AND WEIGHT-OF-EVIDENCE DESCRIPTORS

	TD_{50}	EPA	IARC/HC	NTP	NCI	DSS-Tox
Toxicity Category 1**.	<0.1	Group A; Human Carcinogen.	Group 1	CE 2 species/2 sexes; or 2 species; or 2 sexes.	P 2 species/2 sexes; or 2 species; or 2 sexes.	H.
Toxicity Category 2	0.1–100	Groups B1 and B2; likely carcinogens.	Group 2A	Combinations of CE, SE, EE, and NE.	Combinations of P, E and N.	HM.
Toxicity Category 3	>100	Group C; Suggestive evidence of carcinogenicity.	Group 2B	Combinations of SE, EE, and NE.	Combinations of E and N.	M and LM.

** Cancer data placed chemicals in only the three highest Toxicity Categories.
CE = clear evidence, SE = some evidence, EE = equivocal evidence, NE = no evidence.
P = positive, N = Negative, E = equivocal.
H = high probability, HM = high to medium probability, M = medium probability, LM = medium to low probability.

EPA chose a conservative approach in the screening process to categorize each chemical's toxicity and evaluated all the available health effects dose-response and categorical data elements for a given chemical. Chemicals were assigned to the highest toxicity category indicated after an evaluation of all the available data. Accordingly, if a chemical had just one data element that places it in Toxicity Category 1, it was categorized as such even if some of the other data elements for that same chemical may place it in a lower toxicity category. For ~~example, if a chemical is classified~~ as a 2A carcinogen by IARC, it was placed in Toxicity Category 2 using the descriptive cancer data even if a quantified LOAEL from a different study places it in Toxicity Category 3.

b. Occurrence Data Elements

EPA evaluated the occurrence data elements for each chemical and placed them on the horizontal axis of the screening table. In assessing the data, EPA found that the data elements that represent a chemical's potential to occur in drinking water vary greatly. EPA's goal was to determine which data elements best represented the potential to occur in drinking water. EPA considered and evaluated data elements in the following categories:

- Finished Water—measures of concentration and frequency of detections.
- Ambient Water—measures of concentration and frequency of detections.
- Total Releases in the Environment—pounds per year and number of States.
- Pesticide Application Rates—pounds per year and number of States.
- Production volume—pounds per year.

In addition to evaluating quantitative data elements listed above, EPA also considered chemicals with descriptive data based upon their likelihood of occurring in drinking water. Examples of descriptive occurrence data elements include characterization as a disinfection byproduct or a drinking water treatment chemical.

EPA used the following hierarchal approach to select the occurrence data element used to screen a chemical: Finished Water or Ambient Water > Environmental Release Data > ~~Production Data~~.

The highest data elements in the hierarchy are the finished and ambient water data; the lowest, the production data. Environmental release data from the Toxics Release Inventory (TRI) and pesticide application amounts occupy the middle position in the hierarchy.

EPA also decided that when multiple data values exist for the chemicals within a given component of the hierarchy, the most conservative data value is used. For example, in the case of a chemical that has finished water data and ambient water data, EPA selected the highest reported concentration as the occurrence value used in screening.

EPA obtained the finished water data elements from the National Contaminant Occurrence Database (NCOD), the Unregulated Contaminant Monitoring (UCM) Rounds 1 and 2, the National Inorganic Radionuclides Survey (NIRS), the Unregulated Contaminant Monitoring Regulation (UCMR) monitoring, the Information Collection Rule database for disinfection byproducts, the U.S. Department of Agriculture (USDA) Pesticide Data Program (PDP), and the U.S. Geological Survey (USGS) Pesticides Pilot Monitoring Program (PPMP). These sources included data elements such as percent samples with detections, percent drinking water systems with detections, mean and/or median detected concentrations, and highest observed concentrations.

EPA obtained ambient water values from the USGS National Water Quality Assessment Program (NAWQA), the USGS Toxics Substances Hydrology program's National Reconnaissance of Emerging Contaminants (NREC) and related studies, and the PPMP. These sources included data elements such as ~~percent samples with detections~~, percent sites with detections, mean and/or median detected concentrations, and highest observed concentrations.

The environmental release data are those reported for 2004 from the TRI and the National Pesticide Use Database, developed by the National Center for Food and Agricultural Policy (NCFAP). The available environmental release data elements include: total releases to the environment (lbs/yr), number of States with releases, pesticide total mass active ingredient applied nationally (lbs/yr), and number of States with pesticide application. EPA chose to use the pounds released per year into the environment for screening because the mass applied to the environment was more directly related to a potential concentration in water than the number of States where a chemical is released or applied.

EPA used the Toxic Substances Control Act (TSCA) chemical production volume ranges reported under the Chemical Update System/Inventory Update Rule (CUS/IUR) to assess production volume. EPA selected the most recent year of data available for each particular chemical. CUS/IUR reports chemical production volume ranges rather than as exact values of release, and provides production data for all chemicals produced in volumes exceeding 10,000 lbs/yr. The production data are reported in 5 categories that range from less than 10,000 lbs/yr to greater than 1 billion lbs/yr. Therefore, EPA chose to use those ranges as the occurrence subdivisions for the production data.

The occurrence data were grouped by powers of 10 and arrayed from low to high across the horizontal axis of the screening table (Exhibit 4). The document entitled "CCL 3 Chemicals: Screening to a PCCL" (USEPA, 2008b) describes the analyses in greater detail.

In some cases, disinfection byproducts and water treatment chemicals lacked quantitative data elements in the Universe. However, both groups have a strong potential to be present in drinking water. EPA moved chemicals in these two categories forward to the PCCL for further evaluation even when limited health effects and/or occurrence information were available.

c. Selection of the PCCL

The last step in the screening process used the intersections between health effects and occurrence data elements in the screening table (Exhibit 4) to establish the PCCL selection line. As noted above, the health data elements were grouped by the 5 toxicity categories with the element showing the highest potency determining placement in the screening table. EPA selected the highest available data element in the occurrence hierarchy to determine placement of a chemical on the horizontal axis in the screening table. Because the chemicals were evaluated using a hierarchical approach for their occurrence elements, EPA developed separate criteria for each of the occurrence elements, and used the placement of a group of test chemicals that had all or nearly all of the occurrence data elements, to establish the position of the PCCL selection line. The test chemicals were selected from regulated and past CCL chemicals. Each had data to illustrate whether it was or was not of concern as a drinking water contaminant.

As a secondary analysis, EPA evaluated existing Drinking Water Equivalent Levels (DWELs) to confirm whether they would make the PCCL. The DWELS were derived from the lower RfD potency for each of the RfD Toxicity Categories. The DWEL (mg/L) is calculated from the RfD in mg/kg/day by multiplying the RfD by an adult body weight of 70 kg and dividing by a drinking water intake of 2 L/day (rounded to one significant figure).When comparing the position of the set of DWELs to the PCCL selection line, all four toxicity categories would be put on the PCCL. This analysis supports the position of the PCCL selection line for chemicals with finished or ambient water concentration data.

EPA also used the test chemicals to determine the PCCL selection line for the other occurrence data elements—total releases to the environment (i.e., TRI, pesticide application data) and production data. For example, the test chemicals were placed in Exhibit 4 based on their release data to guide the placement of the line that separated the "pass to the PCCL" chemicals from the "do not pass to the PCCL" chemicals. In general, the PCCL selection line was positioned so that regulated and most prior CCL chemicals would be selected for the PCCL.

EPA also analyzed the test chemicals with respect to occurrence, releases, and production data. The test data fit well for the former two categories. For the latter, the fit was not as good so EPA chose to set the PCCL selection line at the point where all chemicals produced at greater than 100 million pounds per year pass to the PCCL even if they fall in the lowest toxicity category.

The criteria for moving a chemical with finished or ambient water, environmental release, and production data to the PCCL are displayed in Exhibit 7.

EXHIBIT 7.—CRITERIA FOR A CHEMICAL TO PASS SCREENING TO THE PCCL

Health effects	Occurrence (by data type)		
	Finished/ambient water concentrations	Release amount (per year)	Production volume (per year)
Toxicity Category 1	All Concentrations	All Amounts	All Amounts.
Toxicity Category 2	≥1 µg/l	≥10,000 lbs/yr	≥500,000 lbs/yr.
Toxicity Category 3	≥10 µg/l	≥100,000 lbs/yr	≥10 M lbs/yr.
Toxicity Category 4	≥100 µg/l	≥1 M lbs/yr	≥50 M lbs/yr.
Toxicity Category 5	≥1000 µg/l	≥10 M lbs/yr	≥100 M lbs/yr.

EPA added DBPs and drinking water additives that lacked quantitative occurrence data but fell in the Toxicity Category 1 or Toxicity Category 2 groupings to the PCCL because of their high probability for being present in disinfected and treated drinking water.

The screening process provides a data-driven, objective, and transparent process for selecting the PCCL from the Universe. All Toxicity Category 1 chemicals (i.e., most toxic) were captured regardless of their occurrence category. The occurrence threshold required for the PCCL selection became less inclusive as the contaminant toxicity decreased. The screening of the CCL 3 Universe resulted in the selection of 532 chemical contaminants for the PCCL from the approximately 6,000 chemicals that were screened. The categorical summary of chemicals that passed the screening is illustrated in Exhibit 8. A complete chemical PCCL list can be found in Appendix B of the document entitled, "CCL 3 Chemicals: Screening to a PCCL" (USEPA, 2008b). The 532 PCCL chemicals were further scrutinized as part of the next key step in the process. Some of the contaminants on the PCCL had limited data available for the scoring protocols and could not be run through the models. The 32 contaminants that had limited data identified in the appendixes to the "Classification of the PCCL to the CCL" support document (EPA 2008c) and will remain on the PCCL until new data are identified for further evaluation.

EXHIBIT 8.—SUMMARY OF TOTAL CHEMICALS THAT PASSED SCREENING FOR PCCL BY SCREENING CATEGORIES

Toxicity categories	Finished or ambient water concentration	Pesticide app	Total releases	Production volume	Totals
Toxicity Category 1	29	4	56	38	127
Toxicity Category 2	33	26	32	61	152
Toxicity Category 3	36	31	21	66	154
Toxicity Category 4	5	4	10	63	82
Toxicity Category 5	0	0	0	17	17

3. Using Classification Models To Develop the CCL 3

The 532 PCCL chemicals were further scrutinized as part of this key step in the process by using classification models as tools to aid in the selection of the draft CCL 3. As experience is gained, the EPA expects to modify and improve the development of the classification process for future CCLs.

From the inception of the development of the CCL classification process, EPA intended to use classification models as a decision support tool. EPA envisioned that, after testing and evaluation, models would be used to process complex data in a consistent, objective, and reproducible manner and provide a prioritized listing of candidate contaminants for the last stage of the CCL process—an expert review and evaluation. Model application also would help EPA focus resources for the expert review and evaluation of the highest priority potential contaminants.

An overview of the classification model approach used to further evaluate chemicals on the PCCL is described in the following sections. A detailed discussion of the process is provided in a document entitled, "Contaminant Candidate List 3 Chemicals: Classification of the PCCL to the CCL" (USEPA, 2008c). The development of this classification process involves the following steps:

- Development of the Attribute Scoring Protocols.
- Development of the Training Data Set.
- Application of the Classification Models.
- Evaluation of Classification Model Output and Selection of the CCL.

To use models to evaluate and classify the PCCL contaminants for listing on the CCL, EPA needed to develop methods to interrelate the important measures (i.e., attributes) that represent a contaminant's health effects and potential for occurrence in drinking water. Four attributes were selected: Potency, severity, prevalence, and magnitude. Protocols were developed for scoring each attribute.

EPA also tested and evaluated the results of several classification models to determine which ones might provide the best decision support tools. To make this evaluation, EPA developed a chemical data set and used the data set to "train" the classification models. The selected models were utilized to process the data for the PCCL chemicals and provide a prioritized listing of candidate contaminants for the expert review and evaluation.

a. Development of the Attribute Scoring Protocols

EPA used attributes to characterize different chemicals on the basis of similar qualities or traits. These qualities or traits represent the likelihood of occurrence or potential for adverse health effects of each contaminant. Throughout the process of evaluating the attributes EPA recognized that a wide range of data elements would have to be used for each attribute to characterize chemicals on the PCCL. To evaluate PCCL chemicals with differing types of occurrence and health effects data as potential CCL contaminants, one must be able to establish consistent relationships among the different types of data that represent measures of the attributes. If the same data were available for all contaminants, the comparison and prioritization of candidates would be less complex. To consistently apply the best available data for PCCL chemicals, EPA normalized the different types of data into scales and scoring protocols that accept a variety of input data, apply a consistent framework, and compare different types of data. The following sections describe how EPA developed the scales and scoring protocols for the health effects and occurrence attributes.

i. Health Effects Attributes

Potency and severity are the attributes used to describe health effects. EPA defines potency as the lowest dose of a chemical that causes an adverse health effect and severity is based on the adverse health effect associated with the dose used to define the measure of potency. In other words, potency was scored on the dose that produced the adverse effect and severity was scored based on the health-related significance of the adverse effect (*e.g.*, from dermatitis to organ effects to cancer). These two attributes are interrelated, in that the severity is linked to the measure of potency.

The following toxicological parameters were used to evaluate potency:

- Reference Dose (RfD) or equivalent.
- Cancer potency (concentration in water for 10^{-4} cancer risk).
- No-Observed-Adverse-Effect Level (NOAEL).
- Lowest-Observed-Adverse-Effect Level (LOAEL).
- Rat oral median Lethal Dose (LD_{50}).

EPA developed a "learning set" of about two hundred chemicals to calibrate the potency scoring protocols. Once the data for the learning set of chemicals was collected, EPA arrayed and graphically displayed the data to analyze their range and distribution. EPA selected a distribution based on logarithms (base 10) of the toxicity parameters rounded to the nearest integer because it provided a spread of the chemical toxicity parameters across the range and the curve was roughly log-normal.

EPA used a log-based distribution to establish a potency scoring equation for each toxicity parameter. This was accomplished by assigning the most frequent (modal) value in each distribution a score of 5 on a 10 point scale. When the toxicity parameter was one log more toxic than the modal value, a score of 6 was assigned. Similarly, when the parameter was one log less toxic than the modal value a score of 4 was given, and so on. EPA developed an equation for each toxicity parameter that equated the modal value to a score of 5 and calculated the potency score. Because the modal rounded log differed for the different measures of toxicity, it was necessary to use a different equation for each to normalize the mode to a score of 5. The resultant equations are summarized in Exhibit 9.

EXHIBIT 9.—SCORING EQUATIONS FOR POTENCY

RfD Score = 10 − (Log_{10} of RfD + 7).
NOAEL Score = 10 − (Log_{10} of NOAEL + 4).
LOAEL Score = 10 − (Log_{10} of LOAEL + 4).
LD_{50} Score = 10 − (Log_{10} of LD_{50} + 2).
10^{-4} cancer risk Score = 10 − (Log_{10} of the 10^{-4} cancer risk + 6).

For distributions that spanned more than 5 orders of magnitude above or below the mode, scores for the tails of the distribution were truncated at 1 and 10. Conversely, for distributions that did not span 5 full orders of magnitude above and below the mode, not all scores between 1 and 10 were used. For example, the distribution of the 10^{-4} values for cancer risk was skewed, with values up to 5 orders of magnitude above the modal value (more potent carcinogens) but only 2 orders of magnitude below the mode (less potent carcinogens). This meant that the lowest potency score for this toxicity parameter was a "3."

EPA tested the scoring process by using a subset of contaminants with values from multiple data elements considered in the process. In the testing of the potency scoring process, EPA scored all of the chemicals in the learning set for each toxicity parameter to examine the consistency across scores for the non-cancer measures of potency. EPA evaluated the agreement of non-cancer scores across the RfD, NOAEL, LOAEL and LD_{50} inputs and found the scores for any given compound to be generally consistent across parameters. Because of the general consistency among scores, EPA determined that a hierarchy of RfD> NOAEL> LOAEL> LD_{50} would be used in the scoring of potency. This hierarchy gives preference to the potency value with the richest supporting data set (the RfD—or equivalent values) and gives the lowest ranking to the LD_{50} because it is a measure of acute rather than chronic toxicity. If data are available for both the cancer and noncancer endpoints, the higher of the cancer or noncancer potency is selected and the critical effect of the higher measure of potency is used to score the severity.

Severity refers to the relative impact of an adverse health affect. Just as toxicity increases with dose, the severity of the observed effect also increases. A low dose effect could be a simple increase in liver weight while the same chemical at a higher dose could cause cirrhosis of the liver. For consistency, the measure of severity that was used for scoring the PCCL chemicals was the effect or effects seen at the LOAEL. Restricting severity scores to the effects at the LOAEL ties them to the data used to derive the potency score.

The severity measures used to score the PCCL chemicals differ from those used for potency, prevalence, and magnitude because they are descriptive rather than quantitative. Accordingly, they are less amenable to automation and often require more scientific judgment in their application. To guide scoring for severity, EPA developed the nine-point scale displayed in Exhibit 10, and a compendium of nearly 250 descriptions of critical effects grouped by their severity scores (*e.g.*, "Chronic irritation without histopathology changes" equals a score of 3).

EXHIBIT 10.—FINAL NINE-POINT SCORING PROTOCOL FOR SEVERITY

Score	Critical effect	Interpretation
1	No adverse effect.	
2	Cosmetic effects	Considers those effects that alter the appearance of the body ~~without affecting structure or functions~~.
3	Reversible effects; differences in organ weights, body weights or changes in biochemical parameters with minimal clinical significance.	Transient, adaptive effects.
4	Cellular/physiological changes that could lead to disorders (risk factors or precursor effects).	Considers cellular/physiological changes in the body that are used as indicators of disease susceptibility.
5	Significant functional changes that are reversible or permanent changes of minimal toxicological significance.	Considers those disorders in which the removal of chemical exposure will restore health back to prior condition.
6	Significant, irreversible, non-lethal conditions or disorders	Considers those disorders that persist for over a long period of time but do not lead to death.
7	Developmental or reproductive effects	Considers those chemicals that cause developmental effects or that impact the ability of a population to reproduce.
8	Tumors or disorders likely leading to death	Considers chemical exposures that result in a fatal disorder and all types of tumors.
9	Death.	

Severity scores 1 through 6 represent a progression in the severity of the observed effect. Severity score 7 is used for all studies where the effect observed is a reproductive and/or developmental effect allowing the Agency to track the chemicals that pose developmental or reproductive concerns consistent with the 1996 SDWA. A severity score of 8 was used to track all cases where cancer is the basis for the potency score.

ii. Occurrence Attributes

EPA used prevalence and magnitude to describe the potential to occur in drinking water. Prevalence measures how widespread the occurrence of the contaminant is in the environment or how widely the contaminant may be distributed. The prevalence measure indicates the percent of public water systems or monitoring sites across the nation with detections, number of States with releases, or the total pounds produced nationally. Magnitude relates to the quantity of a contaminant that may be found in the environment. The magnitude measures include the median concentration of detections in water or the total pounds of the chemical released into the environment. In most cases the same data element (*e.g.*, detections in drinking water or amount released into the environment) could be used to determine the prevalence, based on the spatial distribution and magnitude based on the amounts. However, where production data were used to determine prevalence, there was no corresponding direct measure of magnitude, so persistence and mobility data were used as surrogate indicators of potential magnitude.

Production/persistence and mobility data are assigned the lowest level in the hierarchy of data available for prevalence and magnitude. Persistence-mobility is determined by chemical properties that measure or estimate environmental fate characteristics of a contaminant and affect their likelihood to occur and persist in the water environment. Data sources that could provide occurrence data ranged from direct measure of concentrations in water to annual measures of environmental release or production. EPA compiled a second subset or learning set of 207 chemicals, with available data for all of the occurrence attribute data elements that measured prevalence and each of the data elements that measured magnitude, to calibrate protocols for prevalence and magnitude.

The data available for the prevalence attribute consisted of measurements of a contaminant's occurrence across the United States. The prevalence measures have finite ranges such as zero to 100 percent of samples/sites or 1 to 50 States depending on the reporting requirements of the available data source. Accordingly, the scaling of scores for prevalence focused on establishing appropriate groupings of the number of sites or States impacted across the 1 to 10 scoring scale.

The relationship between production or even environmental release data and the actual occurrence in drinking water is complex. Where actual water measurements are available, they are the preferred data element to score prevalence because they are the most direct measures of occurrence in drinking water. EPA selected the following hierarchy for scoring prevalence:

- Percent of PWSs with detections (national scale data).
- Percent of ambient water sites or samples with detections (national scale data).
- Number of States reporting application of the contaminant as a pesticide.
- Number of States reporting releases (total) of the chemical.
- Production volume in lbs/yr.

The production data provide the pounds produced annually of a chemical product in the United States. To some extent, this production rate represents the commercial importance of the chemical, so EPA interpreted the high production tonnage as a likely indication of wide use of a commodity chemical and used this information to score prevalence. For example, a chemical produced at a billion lbs/yr is more likely to be used and released more widely than a compound produced at only 10,000 lbs/yr.

Magnitude represents the quantity of a contaminant that may be in the environment. The data sources that provided the first four levels of the prevalence hierarchy provided direct measurements of water and environmental release that could be used to score magnitude. However, the production categories did not supply an appropriate measure for magnitude. EPA used the persistence and mobility for chemicals with only production data as the basis of the magnitude attribute.

To keep the process straightforward, EPA used one scale for all water concentration data. EPA distributed scores across the range of values so that organic contaminants could receive high scores as well as the inorganic contaminants (IOCs). Comparisons and adjustments were made until there was a reasonable distribution of the scores for organic and inorganic contaminants by using a semi-logarithmic scale. EPA selected the single scale approach and this is discussed in more detail in the report entitled "CCL 3 Chemicals: Classification of the PCCL to the CCL" (USEPA, 2008 c).

When developing the calibration scales for the release data, the ranges of data were similarly arrayed using a scale based on half-log units with a distribution of scores that reflected the distribution of the data in the learning set.

EPA based the persistence and mobility scores on chemical and physical properties combined with environmental fate parameters. Persistence and mobility act as measures of potential magnitude because both fate (i.e., persistence) and transport (i.e., mobility) affect the amount of a contaminant to be found in water. The length of time a chemical remains in the environment before it is degraded (persistence) affects its concentration in water. Similarly, the mobility of a chemical, or its ability to be transported to and in water, affects its potential to reach and dissolve in the source waters, and thus, the ultimate concentration of the chemical in the water.

EPA considered a number of data elements to measure the mobility of a chemical in the environment. The physical/chemical parameters that were chosen for the CCL process are:

- Organic Carbon Partition Coefficient (K_{oc})
- Octanol/Water Partition Coefficient (K_{ow})
- Soil/Water Distribution Coefficient (K_d)
- Henry's Law Coefficient (K_H)
- Solubility

The first 4 measures of mobility represent the equilibrium ratio for the partitioning of the contaminant from one medium to another: K_{oc} (soil/sediment organic carbon: water), K_{ow} (octanol: water), K_d (soil/sediment: water) and Henry's Law Coefficient (air: water). K_{oc}, K_{ow} and K_d are sometimes expressed as logs of the original measurements. The measures of persistence reflect the time the chemical will remain unchanged in the environment. Persistence is reflected in the following measures of environmental fate:

- Half-Life
- Measured Degradation Rate
- Modeled Degradation Rate

Each of the mobility and persistence data elements listed above are presented in hierarchical order, with the most desirable at the top (i.e., the first data to be used if available).

As was the case with prevalence, EPA used a hierarchy in scoring magnitude. The hierarchy uses finished water occurrence data if available, and if not, the highest available element in the hierarchy of finished water data > ambient water data > environmental release data > persistence and mobility data. The data elements used in scoring magnitude follow:

- Median value of detections from finished water systems (PWSs) (national scale data)
- Median value of detections from ambient water sites or samples (national scale data)
- Amount of pesticide applied (annual, in pounds)
- Amount of total releases (annual, in pounds)
- Persistence and mobility data

EPA developed attribute scoring protocols through a step-wise process of data selection, data analysis, calibration of scales, and evaluation of the functionality of the scores in PCCL to CCL decision-making. This is discussed in more detail in the report entitled "Contaminant Candidate List 3 Chemicals: Classification of the PCCL to the CCL" (USEPA, 2008 c). EPA used the attribute protocols to normalize the data for the PCCL chemicals and develop a set of scores for the four attributes that are the input into the models. By normalizing the data elements, EPA developed a process that can use different kinds of data and information (e.g., quantitative and descriptive) to develop input to the models and provide a relative score for potential contaminants using the attribute scores.

b. Training Data Set for the Classification Models

The training data set (TDS) for chemicals is the set of data used to train (or teach) the classification models to mimic EPA expert list-not list decisions for PCCL chemicals. EPA compiled this data set in addition to the two learning sets to represent the types of chemicals likely to move forward to the PCCL. This data set also represents the range of possible attribute scores and listing decisions needed to train and calibrate the classification models. The TDS used to train the models for CCL 3 was comprised of 202 discrete sets of attribute scores for chemicals and consensus list-not list decisions made by a team of EPA subject matter experts.

Classification models use statistical approaches for pattern recognition and derive mathematical relationships among input variables (e.g., measurements or descriptive data) and output from a TDS. EPA used classification models to develop a relationship between the contaminant attribute scores (input variables) and the classification of these contaminants into list-not list categories (output). EPA subject matter experts familiar with the technical aspects of the attribute data and the selection of drinking water contaminants for listing and regulation made the list-not list decisions for the TDS. EPA then applied the models to the PCCL to predict likely list-not list decisions.

EPA considered the following key factors in developing the training data set:

- Selection of contaminants representing a range of outcomes and decisions likely to be encountered in developing a CCL;
- A variety of input data ensuring adequate coverage of attribute scores and combinations of scores;
- Chemicals that, when present in drinking water, would present a meaningful opportunity for public health improvement if regulated; and
- Contaminants that would likely be selected for the PCCL.

The TDS used for training the classification models consisted of 202 combinations of attribute scores and the decisions made by EPA experts. The TDS included some of the contaminants from the learning sets used in developing the scoring protocols for toxicity and occurrence. It also included additional contaminants to meet the key factor requirements described above. The set of known chemicals chosen for the TDS was supplemented with a set of attribute scores and decisions that were selected to balance the range of scored attributes the classification model would need to evaluate as described further below.

Initially, EPA selected "data rich" contaminants from among regulated contaminants and previous CCLs because they had a range of readily available occurrence and health effects information. EPA drinking water subject matter experts and stakeholders reviewed the initial list of contaminants and identified additional candidates for the TDS. This initial selection process identified 51 chemical contaminants. Subsequently, EPA randomly chose 50 contaminants from chemicals in the CCL 3 Universe with high health effects potency values and accompanying occurrence data because they represented contaminants likely to make it to the PCCL. The addition of these 50 contaminants resulted in 101 contaminants with data to score attributes.

The performance of the classification models using the initial TDS gave an indication of gaps in the possible attribute space that the set of 101 TDS contaminants did not adequately cover. This led EPA to add the sets of possible attribute scores to the TDS based on Latin hypercube sampling (NIST, 2006; *http://www.itl.nist.gov/div898/handbook/glossary.htm#LHC)*. Using this approach, EPA added 101 specific combinations of attribute scores to fill in gaps in the space defined by total possible attribute scores and improve the performance of the models. This set of 202 scores and decisions ensured good coverage of both "list" and "not list" outcomes and became the TDS. Models trained with the TDS with 202 decisions had greater agreement with EPA subject matter experts than those trained with the TDS of 101 contaminants.

List-not list decisions were a key component of the TDS. EPA subject matter experts made list-not list decisions as individuals and as a group, based on attribute scores and based on data that had not been converted to attribute scores (actual or raw data). The development of the list-not list decisions was an iterative process that incorporated revisions to the attribute scoring protocols as experience was gained by the EPA experts. EPA resolved differences between the decisions based on the scored attributes and the raw data by revising the scoring protocols based on the EPA experts' experience to improve the correlation of decisions based on scores to those based on raw data.

EPA subject matter experts reviewed and evaluated the health effects and occurrence data for each contaminant. Each individual reviewer made decisions about how to classify the contaminant and then met as a group to discuss their decisions. Early in the process the reviewers recognized that clear list or not-list decisions could easily be made for some contaminants, but not for other contaminants. For the chemicals where the decision whether to list contaminants was not clear, two categories were added to the analyses. The categories of List? (L?) or Not List? (NL?) allowed the group to identify chemicals that were close to the boundary for a List-Not List decision. That is L? signifies that the decision is leaning towards listing but with some uncertainty, and NL? signifies that the decision is leaning towards not listing but with some uncertainty. These additional two categories were incorporated into the evaluation and model training process.

The EPA subject matter experts also reached a consensus decision for each contaminant. This consensus decision was used to train the models. This is discussed in more detail in the report entitled "Contaminant Candidate List 3 Chemicals: Classification of the PCCL to the CCL" (USEPA, 2008c).

c. Evaluation of Classification Models

EPA identified several different models for possible use in selecting contaminants from the PCCL for the CCL: Artificial neural networks, classification decision trees, linear models, and multivariant adaptive regression splines. EPA evaluated the classification models in a two-step process. The first step was the evaluation and selection of models from within each of the model classes that best predicted the consensus decisions of the subject matter experts. The second step was the evaluation of the performance of the best models selected from each class (USEPA, 2008c).

EPA evaluated models based on the 4 attributes that the model was able to consider, the types of relationships or mathematical functions that the model utilized, and the model's ability to predict classifications of the TDS. The iterative training process minimized the model's predictive error, thereby reducing incorrect model predictions. EPA also evaluated the impact of the attributes used by the models and the effects of missing data on the performance of the models during the various stages of development.

EPA evaluated the performance of five models. Three models, Artificial Neural Network (ANN), Quick, Unbiased and Efficient Statistical Tree (QUEST), and Linear Regression demonstrated consistent performance when trained and evaluated with the TDS. The classification models were assessed and compared with respect to:

- The number of correct and incorrect classifications for the 202 TDS contaminants.
- The number of "large" misclassifications (off by more than one category).
- The weighted sum of TDS classification errors.
- Ability to identify intermediate classifications.
- Consistent behavior (e.g., no decreasing classification as attribute scores increase).

This is discussed in more detail in the report entitled "Contaminant Candidate List 3 Chemicals: Classification of the PCCL to the CCL" (USEPA, 2008c).

d. Application and Use of Model Results

From the inception of the development of the CCL classification process, EPA intended to use classification models as decision support tools. It was envisioned that the models would be used to process complex data in a consistent, objective, and reproducible manner and provide a prioritized listing of contaminants, allowing EPA to focus resources on the expert review and evaluation of the highest priority potential contaminants. The ANN, Linear, and QUEST models are three different classes of models, with three different mathematical approaches, yet they all provided similar results and logical determinations. EPA explored simple ways to combine the results of all three models, to capture both agreement among models and unique results. Both a straightforward, additive approach, and a collective, rank-order approach were utilized to provide a prioritized listing of contaminants to be considered further and evaluated for possible inclusion on the draft CCL 3.

e. Model Outcome and Expert Evaluation

In the last step of the process, the chemicals on the PCCL were scored for their attributes and evaluated by the three models. Some of the contaminants on the PCCL had limited data available for the scoring protocols and could not be run through the models. The 32 contaminants that had limited data are identified in the appendixes to the "Classification of the PCCL to the CCL" support document (EPA 2008c) and will remain on the PCCL until new data are identified for further evaluation. As part of the evaluation of model output, EPA formulated several post-model refinements that were added to the CCL selection process. Exhibit 11 illustrates the results of the model output for the PCCL contaminants. The PCCL consisted of chemicals with variable health effects data, ranging from reference doses (RfD) to Lethal Dose 50s (LD_{50}), and occurrence data ranging from measured water concentration data from Public Water Systems (PWS) to production volume data.

EXHIBIT 11.—MODEL RESULTS FOR THE PCCL CHEMICALS

3-Models decision	% of PCCL	Total # PCCL	Finished or ambient water	Release	Production
L	9	44	3	24	17
L–L?	12	58	9	29	20
L?	33	163	26	64	73
NL?–L?	6	30	6	11	13
NL?	28	139	29	28	82
NL?–NL	4	20	7	9	4
NL	9	46	21	7	18
N (all)	100	500	101	172	227

Four of the seven decision categories, L, L?, NL?, NL, in the first column of Exhibit 11 signify that all of the models were in unanimous agreement with the listing decision. The other categories (e.g., NL?–L?) represent varied agreement where one or two of the models chose one category and the other model(s) resulted in a different category. Note that none of the models placed a contaminant in a category more than one category higher or lower than the other models. That is, no contaminants were categorized as "L" by one model and as "NL?" by one of the other models, or visa versa. The models categorized approximately one-half of the chemicals on the PCCL as L? or above. When analyzed by data type, the majority of chemicals in the List category used LD_{50} data for health effects. This was a concern and became an important issue for consideration. The role LD_{50} played in the health effects scoring was discussed extensively during the post-model evaluation process.

As part of the last stage in the CCL classification process, the model output was reviewed by a group of internal EPA experts representing several offices. This step involved a detailed review of the data used for the models and the available supplemental data for the chemicals. The EPA experts also deliberated on the method of using the model data to produce a draft proposal for CCL 3. The function of this review was to critically compare the results from the model to the data for the chemicals for a cross section of the modeled contaminants.

Based upon issues identified by the evaluators, several post model refinements were added to the CCL process. Three major issues and refinements are described below.

The relationship between potency and concentration was important when deciding whether to list a chemical. However this ratio could only be developed when water concentration data were available. Accordingly, calculation of the ratio between the health-based value and the 90th percentile concentration in finished or ambient water was added as a post-model process. The potency/concentration ratio serves as a benchmark that suggests a greater concern for a contaminant if the ratio is low and a lesser concern when it is high.

The addition of modeled occurrence data for pesticides and estimated concentration in surface and ground water was obtained from the EPA Office of Pesticide Programs (OPP). The modeled estimates of concentration in water for pesticides are part of the EPA's pesticide registration and re-registration evaluations. Once the availability of the OPP data for some of the pesticides was confirmed, the data were extracted from OPP documents and used to generate a potency/concentration ratio similar to that used with the water concentration data.

Data certainty was factored into the decision process by characterizing health effect and occurrence data elements and their relative certainty based upon the type of data that was used to score the attribute for the model classification. This characterization tagged data elements with high certainty and low certainty. The combined certainty measure for a single contaminant (i.e., health effects and occurrence tags) was used to place contaminants in bins of high, medium and low certainty.

The high certainty bin consisted of chemicals with direct occurrence measured in water and well-studied data for health effects. Such contaminants are expected to be good candidates for regulatory determination because they provide information that can be considered in that process and have minimal research needs. Examples of the data used to characterize chemicals in the high certainty bin include chemicals with RfDs, LOAELs, and NOAELs, and water concentration data. The medium bin consists of chemicals that will need further occurrence and/or health effects research. For example, chemicals with well studied health effects that only have environmental release data are included in the medium bin. Chemicals that are released to the environment and need further health effects research are also included in the medium bin. The low certainty bin consists of chemicals that have limited data, yet these data suggest that further evaluation should be pursued. These chemicals may need extensive health effects and occurrence research that may require significant resources before regulatory determinations can be made. Examples include chemicals with only LD_{50} and/or production volume data. The CCL should consist both of chemicals that provide sufficient data to support regulatory determinations as well as chemicals that are of concern and need to be targeted for additional drinking water research. Contaminants from each bin were scrutinized separately in selecting which ones should be listed on the CCL 3.

4. Selection of the Draft CCL 3—Chemicals

The chemicals for the draft CCL 3 were selected from within the three certainty bins with the emphasis placed on the source of the occurrence data (e.g., measured concentrations, release, and production). Four groups of chemicals were placed on the CCL based on their modeled scores, the potency-concentration ratios, where available, and the estimate of data certainty. They included:

- 36 chemicals in the high certainty bin with finished or ambient water data and a potency/90th percentile concentration ratio ≤10.
- 24 pesticide chemicals in the medium certainty bin with modeled surface and/or ground water data that yielded a potency/concentration ratio ≤10.
- 27 chemicals in the medium certainty bin with release data that gave modeled L or L-L? rankings.
- 8 chemicals in the low certainty bin that were added to the CCL as recommended by the public in response to EPA's **Federal Register** notice (71 FR 60704, USEPA, 2006b). The notice requested that the public submit chemical and microbial contaminant nominations that should be considered for CCL 3. This process is discussed in section III.C.1.

The potency and concentration were compared to develop a ratio that was used to select contaminants for the draft CCL 3 from the high certainty bin. A ratio between the health-based value and the 90th percentile was taken for chemicals with measurements in finished and ambient water. Contaminants for this bin were selected for the draft CCL 3 when the ratio was ≤10, representing occurrence in water at a level of concern related to its health effects data.

The pesticides in the medium bin, where modeled data was obtained from OPP, were selected for the draft CCL 3 based on their potency/concentration ratios. Similar to the chemicals in the high certainty bin, pesticides were selected for the draft CCL 3 when the potency/concentration ratio was <10, representing potential occurrence in water at a level of concern related to its health effects data. The other chemicals in the medium bin were selected for the draft CCL 3 based on a review of their data and their prioritization from the classification models.

Chemicals in the low certainty bin were selected for the draft CCL 3 based on a review of their supplemental data and the data submitted through the nominations process. Some of the chemicals identified through the nominations process were already on the draft CCL 3 based on the data EPA collected for the universe. The supplemental data provided with the nominations were used to screen the nominated chemicals and score the attributes for those that passed the screen. The scored attributes were then processed through the models and the post-model evaluations. Those that were listed demonstrated adverse health effects and a potential to occur in PWSs. Chemicals not selected for the draft CCL 3 will remain on the PCCL until additional occurrence or health effects data become available to support their reevaluation.

B. Classification Approach for Microbial Contaminants

As discussed in CCL 2 (USEPA, 2005b), the Agency evaluated the NDWAC, NRC and other recommendations, and used the information to develop a pragmatic approach for classifying the microorganisms on the draft CCL 3. The CCL 3 approach for microbes, like the approach used for chemicals, uses the attributes of occurrence and health effects to select the microbial contaminants. EPA's objective is to target microorganisms with the highest potential for human exposure and the most serious adverse health effects. Parallel to the chemical selection process, the Agency considers a broad universe of microbial contaminants and systematically narrows that universe down to develop the draft CCL 3 in a transparent and scientifically sound CCL process. The first step of the CCL 3 approach for microbes identifies a universe of potential drinking water contaminants. The second step screens that universe of microbiological contaminants to a Preliminary Contaminant Candidate List (PCCL). Lastly, EPA selects the draft CCL 3 microbial list by ranking the PCCL contaminants based on occurrence in drinking water (including waterborne disease outbreaks) and human health effects.

1. Developing the Universe

EPA defined the microbial Universe for the draft CCL 3 as all known human pathogens. The Universe process began with the list of 1,415 recognized human pathogens compiled by Taylor *et al.* (2001). The Agency added organisms to the Universe and updated nomenclature in Taylor *et al.* (2001) to account for emerging pathogens and new taxonomy research.

As EPA reviewed Taylor *et al.* (2001), additional pathogens were also identified. EPA surveyed fungi in drinking water and identified six fungi reported to occur in drinking water distribution systems that did not appear on the Taylor list. The added fungi are shown in Exhibit 12. EPA also added reovirus to the Universe based on additional health effects information (Tyler, *et al.*, 2004).

In October 2006, EPA published a notice (71 FR 60704 (USEPA, 2006b)) requesting chemical and microbial contaminant nominations as part of the process to identify emerging contaminants that should be considered for the CCL. As a result of the nominations process, 24 microbial contaminants were nominated by the public. Twenty-two of the microbes were previously identified by Taylor *et al.* (2001) and are already in the Universe. The two additional pathogens nominated were *Methylobacterium* (with two species) and Mimivirus. These two bacterial species, two viral groups and six fungal species were added to the Microbial Universe which brings the Microbial Universe list to 1,425 pathogens. The full Universe list is available in the document, "Contaminant Candidate List 3 Microbes: Identifying the Universe" (USEPA, 2008d).

EXHIBIT 12.—FUNGI ADDED TO THE MICROBIAL UNIVERSE

Pathogen
Arthrographis kelrae
Chryosporium zontatum
Geotrichum candidum
Sporotrichum pruinosum
Stachybotrys chartarum
Stemphylium macrosporoideum

2. The Universe to PCCL

EPA developed screening criteria to reduce the Universe of all human pathogens to just those pathogens that could be transmitted through drinking water. For example, pathogens transmitted solely by animals, such as the virus that causes rabies, were screened out of the Universe and are not included on the PCCL. Screening is based on a pathogen's epidemiology, geographical distribution, and biological properties in their host and in the environment. EPA moved pathogens forward to the PCCL if there was any evidence linking a pathogen to a drinking water-related disease. The screening criteria restrict the microbial PCCL to human pathogens that may cause drinking water-related diseases resulting from ingestion of, inhalation of, or dermal contact with drinking water. EPA used 12 screening criteria (Exhibit 13) to reduce the pathogens in the microbial CCL universe to the PCCL.

EXHIBIT 13.—CCL SCREENING CRITERIA FOR PATHOGENS

1. All anaerobes.
2. Obligate intracellular fastidious pathogens.
3. Transmitted by contact with blood or body fluids.
4. Transmitted by vectors.
5. Indigenous to the gastrointestinal tract, skin and mucous membranes.
6. Transmitted solely by respiratory secretions.
7. Life cycle incompatible with drinking water transmission.
8. Drinking water-related transmission is not implicated.
9. Natural habitat is in the environment without epidemiological evidence of drinking water-related disease.
10. Not endemic to North America.
11. Represented by a pathogen for the entire genus or species (that are closely related).
12. Current taxonomy changed from taxonomy used in Universe.

Pathogens meeting any single criterion of the 12 criteria were removed from further consideration and not moved forward to the PCCL. Based upon this screening exercise, 1,396 of the 1,425 pathogens were excluded and 29 pathogens moved on to the PCCL. The results of the screening process are summarized in Exhibit 14. The screening criteria and results of the screening process are discussed in greater detail in the supporting document titled "Contaminant Candidate List 3 Microbes: Screening to the PCCL" (USEPA, 2008 e).

EXHIBIT 14.—APPLICATION OF TWELVE SCREENING CRITERIA TO PATHOGENS IN THE MICROBIAL CCL UNIVERSE

Pathogen class	Total	Screening Criteria												Pathogens screened out	On PCCL
		1	2	3	4	5	6	7	8	9	10	11	12		
Bacteria	540	125	14	10	37	117	7	0	29	154	2	28	5	528	12
Viruses	219	0	0	26	104	0	19	1	18	0	36	8	0	212	7
Protozoa	66	0	0	1	29	3	0	4	7	7	0	6	0	57	7[*]
Helminths	287	0	0	0	25	0	0	106	0	0	156	0	0	287	0
Fungi	313	0	0	0	0	12	1	0	0	297	0	0	0	310	3
Total	1,425	125	14	37	195	132	27	111	54	458	194	42	5	1,394	29[*]

[*] Two additional protozoa, *Cryptosporidium* and *Giardia* were not considered for CCL 3 and they are discussed in more detail later.

3. The PCCL to Draft CCL Process

Pathogens on the PCCL were scored for placement on the draft CCL. EPA devised a scoring system to assign a numerical value to each pathogen on the PCCL.

Each of the pathogens on the PCCL was scored using three scoring protocols, one protocol each for waterborne disease outbreaks (WBDO), occurrence in drinking water, and health effects. The higher of the WBDO score or the occurrence score is added to the normalized health effects score to produce a composite pathogen score. Pathogens receiving high scores were considered for placement on the CCL.

EPA normalized the health effects score so that occurrence and health effects have equal value in determining the ranking of the CCL. The equal weighting of occurrence and health effects information closely mirrors the risk estimate methods used by EPA during drinking water regulation development. This scoring system prioritizes and restricts the number of pathogens on the CCL to only those that have been strongly associated with drinking water-related disease. Pathogens that scored low will remain on the PCCL until additional occurrence data, epidemiological surveillance data, or health effects data become available to support their reevaluation. It is important to note that pathogens for which there are no data documenting a waterborne disease outbreak in drinking water earn a low score under the protocols. EPA believes that pathogens that have caused a WBDO and have health effects data should rank higher than pathogens that have only data on health effects but no evidence of a WBDO. The following sections describe the three protocols used to score the pathogens on the PCCL and the process by which the scores are combined.

a. Waterborne Disease Outbreak Protocol

The Centers for Disease Control and Prevention (CDC), EPA and the Council of State and Territorial Epidemiologists (CSTE) have maintained a collaborative surveillance system for collecting and periodically reporting data related to occurrences and causes of WBDOs since 1971. EPA used the CDC surveillance system as the primary source of data for the waterborne disease outbreaks protocol. Reports from the CDC system are published periodically in *Morbidity and Mortality Weekly Report* (MMWR).

For this protocol (Exhibit 15), a pathogen is scored as having a WBDO(s) in the U.S. if that pathogen is listed in a CDC waterborne disease drinking water surveillance summary (i.e., in the MMWR). A pathogen with multiple WBDOs listed by CDC is given the highest score under this protocol. EPA also scored non-CDC reported WBDOs and WBDOs outside the U.S. as well; however these were given lower scores. WBDOs outside the U.S. were scored when information was available from World Health Organization publications or other peer-reviewed publications.

In addition, CDC and EPA acknowledge that the WBDOs reported in the surveillance system represent only a portion of the burden of illness associated with drinking water exposure (CDC, 2004). The surveillance information does not include endemic waterborne disease risks, nor are reliable estimates available of the number of unrecognized WBDOs and associated cases of illness. Therefore, EPA also considered data as indicating a WBDO (even though CDC does not list a WBDO in their MMWR) if the non-CDC data showed a link between human illness defined by a common water source, a common time period of exposure and/or similar symptoms. EPA also considered the use of molecular typing methods to link patients and environmental isolates.

Only two pathogens were given a WBDO score on this basis, *Mycobacterium avium* and *Arcobacter butzlerei*. They are discussed in greater detail in the "Contaminant Candidate List 3 Microbes: PCCL to CCL Process" (USEPA, 2008 f).

EXHIBIT 15.—WATERBORNE DISEASE OUTBREAK SCORING PROTOCOL

Category	Score
Has caused multiple (2 or more) documented WBDOs in the U.S. since CDC surveillance initiated in 1973	5
Has caused at least one documented WBDO in the U.S. since CDC surveillance initiated in 1973	4
Has caused documented WBDOs at any time in the U.S.	3
Has caused documented WBDOs in countries other than the U.S.	2
Has never caused WBDOs in any country, but has been epidemiologically associated with water-related disease	1

b. Occurrence Protocol

The second attribute of the scoring process evaluates the occurrence of a pathogen in drinking water. Because water-related illness may also occur in the absence of recognized outbreaks, EPA scored the occurrence (direct detection) of microbes using cultural, immunochemical, or molecular detection of pathogens in drinking water under the Occurrence Protocol (Exhibit 16). Occurrence characterizes pathogen introduction, survival, and distribution in the environment. Occurrence implies that pathogens are present in water and that they may be capable of surviving and moving through water to produce illness in persons exposed to drinking water by ingestion, inhalation, or dermal contact.

Pathogen occurrence is considered broadly to include treated drinking water, and all waters using a drinking water source for recreational purposes. This attribute does not characterize the extent to which a pathogen's occurrence poses a public health threat from drinking water exposure. Because viability and infectivity cannot be determined by non-cultural methods, the public health significance of non-cultural detections is unknown.

EXHIBIT 16.—OCCURRENCE SCORING PROTOCOL FOR PATHOGENS

Category	Score
Detected in drinking water in the U.S.	3
Detected in source water in the U.S.	2
Not detected in the U.S.	1

c. Health Effects Protocol

EPA's health effects protocol evaluates the extent or severity of human illness produced by a pathogen across a range of potential endpoints. The seven-level hierarchy developed for this protocol (Exhibit 17) begins with mild, self-limiting illness and progresses to death.

The final outcome of a host-pathogen relationship resulting from drinking water exposure is a function of viability, infectivity, and pathogenicity of the microbe to which the host is exposed and the host's susceptibility and immune response. SDWA directs EPA to consider subgroups of the population at greater risk of adverse health effects (i.e., sensitive populations) in the selection of unregulated contaminants for the CCL. Sensitive populations may have increased susceptibility and may experience increased severity of symptoms, compared to the general population. SDWA refers to several categories of sensitive populations including the following: children and infants, elderly, pregnant women, and persons with a history of serious illness.

Health effects for individuals with marked immunosuppression (e.g., primary or acquired severe immunodeficiency, transplant recipients, individuals undergoing potent cytoreductive treatments) are not included in this health effects scoring. While such populations are considered sensitive subpopulations, immunosuppressed individuals often have a higher standard of ongoing health care and protection required than the other sensitive populations under medical care. More importantly, nearly all pathogens have very high health effect scores for the markedly immunosuppressed individuals; therefore there is little differentiation between pathogens based on health effects for the immunosuppressed subpopulation.

This protocol scores the representative or common clinical presentation for the specific pathogen for the population category under consideration. EPA used recently published clinical microbiology manuals as the primary data source for the common clinical presentation. These manuals take a broad epidemiological view of health effects rather than focusing on narrow research investigations. The one exception to this approach was EPA's scoring of health effects for *Helicobacter pylori*. *H. pylori* is discussed in greater detail in section IV.C as well as in the support document, "CCL 3 Microbes: PCCL to CCL Process" (USEPA, 2008 f).

To obtain a representative characterization of health effects in all populations, EPA evaluated separately the general population and these four sensitive populations as to the common clinical presentation of illness for that population. EPA added the general population score to the highest score among the four sensitive subpopulations for an overall health effects score. The resulting score acknowledges that sensitive populations have increased risk for waterborne diseases.

EXHIBIT 17.—HEALTH EFFECTS SCORING PROTOCOL FOR PATHOGENS

Outcome category	Score	Manifestation in population class				
		General population	Children/ infants	Elderly	Pregnant women	Chronic disease
Does the organism cause significant mortality (> 1/1,000 cases)?.	7					
Does the organism cause pneumonia, meningitis, hepatitis, encephalitis, endocarditis, cancer, or other severe manifestations of illness necessitating long term hospitalization (> week)?.	6					
Does the illness result in long term or permanent dysfunction or disability (e.g., sequelae)?.	5					
Does the illness require short term hospitalization? (< week)?	4					
Does the illness require physician intervention?	3					
Is the illness self-limiting within 72 hours (without requiring medical intervention)?.	2					
Does the illness result in mild symptoms with minimal or no impact on daily activities?.	1					

d. Combining Protocol Scores to Rank Pathogens

EPA scored and ranked the PCCL using the three attribute scoring protocols, occurrence, waterborne disease outbreaks, and health effects. These protocols are designed in a hierarchical manner so that each pathogen is evaluated using the same criteria and the criteria range for each protocol varies from high significance to low significance. The three attribute scores are then combined into a total score.

EPA scored pathogens first using the WBDO and occurrence protocols, and then selected the highest score. Selection of the higher score from the WBDO or occurrence protocol elevates pathogens that have been detected in drinking water or source water in the U.S. (occurrence score of 2 or 3) above pathogens that have caused WBDOs in other countries but not in the U.S. (WBDO score of 2).

The CCL selection process considered pathogens causing recent waterborne outbreaks more important than pathogens detected in drinking water without documented disease from that exposure. Direct detection of pathogens indicates the potential for waterborne transmission of disease. Documented waterborne disease outbreaks provide an additional weight of evidence that illness was transmitted and that there was a waterborne route of exposure. EPA developed protocols to define a hierarchy of the relevance that each of these types of data provide in evaluating microbes for the CCL. Combining these two sources of occurrence information enabled EPA to consider both emerging pathogens, which are detected in water and should be considered, yet are not tracked by public health surveillance programs, and those pathogens with WBDO data. This hierarchy also acknowledges that organisms identified as agents in WBDO are a higher priority for the CCL.

Next, pathogens were scored using the Health Effects Protocol. All five population categories were scored for each pathogen using the most common clinical presentation for the specific pathogen for the population category under consideration. Because it is recognized that pathogens may produce a range of illness from asymptomatic infection to fulminate illness progressing rapidly to death, scoring decisions are based upon the more common clinical presentation and clinical course for the population under consideration, rather than the extremes. The pathogen's score for the general population is added to the highest score among the four sensitive populations to produce a sum score between 2 and 14.

Finally, EPA normalizes the Health Effects and WBDO/Occurrence score because the Agency believes they are of equal importance. The highest possible ~~score for WBDO/Occurrence is 5 and the~~ highest possible Health Effect score is 14. To equalize this imbalance, the Agency multiplies the health effects score by $\frac{5}{14}$. Combining health effects data with the WBDO/occurrence data by adding the scores from these protocols provides a system that evaluates both the severity of potential disease and the potential magnitude of exposure through drinking water.

Exhibit 18 presents the scores for all the PCCL pathogens with the exception of *Giardia* and *Cryptosporidium*. These two protozoan pathogens made it through the screening protocol, however, EPA chose not to score or include them on the PCCL because EPA has recently published a national primary drinking water regulation that specifically addresses these pathogens (January 4, 2006, 71 FR 388 (USEPA, 2006 a) and is discussed in more detail later.

EXHIBIT 18.—PATHOGENS ON THE PCCL

Pathogen	WBDO	Occurrence	Normalized health score	Total[1] score
Naegleria fowleri	4	3	5.0	9.0
Legionella pneumophila	5	3	3.6	8.6
Escherichia coli (0157)	5	3	3.2	8.2

EXHIBIT 18.—PATHOGENS ON THE PCCL—Continued

Pathogen	WBDO	Occurrence	Normalized health score	Total[1] score
Hepatitis A virus	5	2	3.2	8.2
Shigella sonnei	5	3	3.2	8.2
Helicobacter pylori	1	3	5.0	8.0
Campylobacter jejuni	5	3	2.5	7.5
Salmonella enterica	5	3	2.5	7.5
Caliciviruses	5	3	2.1	7.1
Entamoeba histolytica	5	3	2.1	7.1
Vibrio cholerae	5	3	2.1	7.1
Adenovirus	2	3	3.6	6.6
Enterovirus	2	3	3.6	6.6
Cyclospora cayetanensis	4	1	2.5	6.5
Mycobacterium avium	4	3	2.5	6.5
Rotavirus	4	2	2.5	6.5
Yersinia enterocolitica	5	3	1.4	6.4
Arcobacter butzleri	4	3	2.1	6.1
Fusarium solani	1	3	2.9	5.9
Plesiomonas shigelloides	4	3	1.8	5.8
Hepatitis E virus	2	1	3.6	5.6
Toxoplasma gondii	2	1	3.2	5.2
Aspergillus fumigatus group	1	3	2.1	5.1
Exophiala jeanselmei	1	3	2.1	5.1
Aeromonas hydrophila	1	3	1.8	4.8
Astrovirus	2	2	1.4	3.4
Microsporidia	1	2	1.4	3.4
Isospora belli	2	0	1.1	3.1
Blastocystis hominis	1	0	0.7	1.7

1. Total Score = Normalized Health Score + the higher of WBDO or Occurrence scores.

e. Other Criteria Considered for Listing and Scoring Microbes on the Draft CCL 3

i. Organisms Covered by Existing Regulations

EPA considered an additional screening criterion based upon contaminants that might be controlled through drinking water monitoring requirements under the Total Coliform Rule (TCR) (54 FR 27544, June 29, 1989 (USEPA, 1989b)). Many of the bacteria in the CCL Universe, including the *Enterobacteriaceae* and members of the genera *Campylobacter* and *Vibrio*, are associated with fecal contamination and as such their presence could be signaled by the total coliform monitoring requirements under current drinking water regulations. In the TCR, EPA chose to require monitoring for *Escherichia coli* or fecal coliform (and total coliforms) in finished drinking water because it provides a broad indication of the potential presence of fecal pathogens in drinking water, though more so for bacteria than for viruses and protozoa.

EPA chose not to exclude common enteric bacterial pathogens from the PCCL even though they may be indicated by the TCR. Numerous waterborne disease outbreaks have occurred in systems that were in compliance with drinking water monitoring requirements under the TCR. EPA recognizes the frequency of total coliform monitoring under the TCR may be limited, especially for smaller systems, thus transitory fecal contamination could go undetected. The recognition of these bacterial pathogens on the CCL list will provide additional understanding of the risks posed by distribution systems.

The Agency is currently revising the TCR and considering distribution water quality issues (because of the pathways of potential fecal contamination). Including these pathogens on the CCL emphasizes their importance in protecting public health. EPA believes that enteric pathogens should be included for further specific regulatory consideration in the CCL.

ii. Organisms Covered by Treatment Technique Regulations

According to SDWA (section 1412(b)(1), as amended in 1996), EPA must select CCL contaminants that "at the time of publication, are not subject to any proposed or promulgated national primary drinking water regulation * * *." In promulgating regulations for contaminants in drinking water, EPA can set either a legal limit (MCL) and require monitoring for the contaminant in drinking water or, for those contaminants that are difficult to measure, EPA can establish a treatment technique requirement. The Surface Water Treatment Rule (SWTR) (54 FR 27486, June 29, 1989 (USEPA, 1989a)) included MCLGs for *Legionella, Giardia,* and viruses at zero because any amount of exposure to these contaminants represents some public health risk. Since measuring disease-causing microbes in drinking water is not considered to be feasible, EPA established treatment technique requirements for these contaminants. The purpose of subsequent treatment technique requirements (Interim Enhanced Surface Water Treatment Rule (63 FR 69478; USEPA 1998a), Long Term Surface Water Treatment Rule 1 (67 FR 1813; USEPA, 2002a) and the Long Term Surface Water Treatment Rule 2 (71 FR 654; USEPA, 2006a)) which included an MCLG of zero for *Cryptosporidium,* is to reduce disease incidence associated with *Cryptosporidium* and other pathogenic microorganisms in drinking water. These rules apply to all public water systems that use surface water or ground water under the direct influence of surface water.

The Ground Water Rule (71 FR 65573, (USEPA, 2006c)) set treatment technique requirements to control for viruses (and pathogenic bacteria) because it was not feasible to monitor for viruses (or pathogenic bacteria) in drinking water. Under the GWR, if systems detect total coliforms in the distribution system, they are required to monitor for a fecal indicator (*E. coli,* coliphage, or enterococci) in the source water. If fecal contamination is found in the source water, the system must take remedial action to address contamination.

While *Cryptosporidium* and *Giardia* have been implicated in WBDOs, there is a substantial amount of research regarding health effects and sensitivity to various treatment control measures. More importantly, as noted above, EPA has recently published a National Primary Drinking Water Regulation, The Long Term 2 Surface Water Treatment Rule that specifically addresses these pathogens (71 FR 654 (USEPA, 2006a)). Therefore, they are excluded from the CCL.

EPA did not exclude specific viruses and *Legionella* from consideration for the CCL even though they have broad category MCLGs and treatment technique requirements. Viruses include a wide range of taxa. The treatment and health effects information for different viral taxa was very limited when setting the treatment technique requirements for surface water and ground water systems. Also, different viral taxa have been implicated in various waterborne disease outbreaks for which EPA did not have dose response or treatment data when promulgating its treatment technique requirements. *Legionella* has recently been identified in numerous WBDOs (e.g., CDC *MMWR* reports, 2006). Additionally EPA received additional information on the occurrence of *Legionella* in distribution systems as part of the nominations process (USEPA 2008g). Therefore EPA included viruses and *Legionella* on the draft CCL 3.

iii. Applying Genomic and Proteomic Data to Microbes

The Agency and NDWAC workgroup evaluated the possibility of using genomics and proteomics as data to identify emerging waterborne pathogens, opportunistic microorganisms, and other newly identified microorganisms. While the application of these data in identifying genetic properties that may be pathogenic is a powerful tool for the elucidation of pathogenic mechanisms, the technology is yet largely unproven and the Agency has decided at this time not to use these techniques for CCL application. However, the Agency is monitoring the progress of these technologies and as the data improve and genomics progresses the Agency may consider them for future CCL development.

4. Selection of the Draft CCL 3 Microbes From the PCCL

The 29 PCCL pathogens in Exhibit 18 are ranked according to an equal weighting of their summed scores for normalized health effects and the higher of the individual scores for WBDO and occurrence in drinking water. EPA believes this ranking indicates the most important pathogens to consider for the draft CCL 3. To determine which of the 29 PCCL pathogens should be the highest priority for EPA's drinking water program and included on the draft CCL 3, the Agency considered both scientific and policy factors. The factors included the PCCL scores for WBDO, occurrence, and health effects; comments and recommendations from the various expert panels; the specific intent of SDWA; and the need to focus Agency resources on pathogens to provide the most effective opportunities to advance public health protection. After consideration of these factors, EPA has determined that the draft CCL 3 will include the 11 highest ranked pathogens shown in Exhibit 18.

Additionally, the Agency notes that, and as can be observed in Exhibit 18, there are a few "natural" break points in the ranked scores for the 29 pathogens, with the top 11 forming the highest ranked group of pathogens. EPA does believe that the overall rankings strongly reflect the best available scientific data and high quality expert input employed in the CCL selection process, and therefore should be important factors in helping to identify the top priority pathogens for the draft CCL 3.

C. Public Input

1. Nominations and Surveillance

On October 16, 2006, EPA published a **Federal Register** notice (71 FR 60704 (USEPA, 2006 b)) requesting the public to submit chemical and microbial contaminant nominations that should be considered for CCL 3. EPA evaluated nominated contaminants to identify the data supporting their nomination. This section describes EPA's request for contaminants and summarizes the nominations received by EPA. A more detailed discussion of the contaminants, including a list of the specific contaminants nominated, can be found in the CCL 3 Nominations Summary in EPA's Water Docket (USEPA, 2008 g).

The Agency sought CCL nominations for contaminants by framing the SDWA requirements in a series of questions to document the anticipated or known occurrence in PWS(s) and adverse health effects of potential contaminants. The Agency requested that the public respond to these questions and provide the documentation and rationale for including a contaminant for consideration in the CCL process. The questions posed to the public were:

—What are the contaminant's name, CAS number, and/or common synonym (if applicable)?

—What factors make this contaminant a priority for the CCL 3 process (e.g., widespread occurrence; anticipated toxicity to humans; potentially harmful effects to susceptible populations (e.g., children, elderly and immunocompromised); potentially contaminated source water (surface or ground water), and/or finished water; releases to air, land, and/or water; contaminants manufactured in large quantities with a potential to occur in source waters)?

—What are the significant health effects and occurrence data available, which you believe supports the CCL requirement(s) that a contaminant may have an adverse effect on the health of persons and is known or anticipated to occur in public water systems?

The Agency compiled the information from the nominations process to identify the contaminants nominated and the rationale for the nomination and to compare the supporting data to information already gathered by EPA.

The nominations process identified 150 chemical and 24 microbial contaminants from 11 organizations and individuals. The organizations that nominated contaminants are:

—American Society of Microbiology (ASM),

—American Water Works Association (AWWA),

—Association of Metropolitan Water Agencies (AMWA),

—Association of State Drinking Water Administrators (ASDWA),

—Mothers Against *Acanthamoeba* Disease,

—Natural Resources Defense Council, (NRDC),

—Riverkeepers,

—State of New Jersey Department of Environmental Protection,

—State of New York Department of Health, and

—State of Texas Commission on Environmental Quality.

Exhibit 19 summarizes the types of nominated contaminants and who nominated them. The complete list of chemical and microbial contaminants nominated can be found in EPA's Water Docket. Some of the nominations identified categories of contaminants that the Agency should consider for the CCL. There were 23 chemical groups identified from the 150 chemical contaminants that were nominated. For example, several organizations identified pesticides that are not currently regulated under the SDWA as candidates for consideration. Other groups identified by the public are listed in Exhibit 19.

EXHIBIT 19.—SUMMARY OF CCL 3 NOMINATIONS

Nominator	Number of individual contaminants or specific examples from nominated groups	Types and groups of contaminants
ASM	2	Mimivirus, *Naegleria fowleri.*
AMWA	3	Nitrosoamines and other DBPs.
ASDWA	14	Disinfection byproducts (DBPs), unregulated pesticides, solvents, total petroleum hydrocarbons, cyanotoxins, 3 perfluorinated contaminants (PFCs), viruses, phthalates, nitrite, nitrate; endocrine disruptors.
AWWA	38	DBPs, pesticides, 16 specific microbes, cyanotoxins, radium, 1,4-dioxane.
Mothers Against *Acanthamoeba* Disease	1	*Acanthamoeba.*
New Jersey DEP	4	PFOS, PFOA, trichloropropane, tertiary butyl alcohol.
New York DOH	24	Pharmaceuticals, personal care products, DBPs, fuel oxygenates, 1,4-dioxane, herbicides, bio-monitoring data.
NRDC	26	Alkylphenolpolyethoxylates (APEs that may be endocrine disrupter compounds (EDC)), all unregulated pesticides, perchlorate, Mycobacterium avium complex (MAC), phthalates, managanese, bisphenol A.
Riverkeeper	52	Pharmaceuticals, sodium, chloride.
Texas DEQ	3	Viruses, nitrite, nitrate.

The Agency evaluated the nominations to identify contaminants not previously considered for the CCL and new pertinent information provided by the public. Nominated contaminants were evaluated to identify and compare supporting information provided to that used in the CCL process. Of the 174 chemical and microbial contaminants nominated, 152 contaminants were already being considered by the Agency. Seven of the nominated contaminants are currently regulated in PWSs and will not be included in the CCL 3 process. Most of the data sources cited in the nominations process were already identified for the CCL 3 process. The nominations process did identify recently published specialized studies from scientific literature that were subsequently incorporated in the CCL 3 evaluation process.

Where new supplemental data was provided for contaminants that had not been identified for the draft CCL 3, EPA used the supplemental data to screen the nominated chemicals and score the attributes for those that passed the screen. EPA then processed the nominated contaminants through the models and the post-model evaluations. Twenty of the contaminants identified in the nominations process are on the draft CCL 3.

2. External Expert Review and Input

EPA actively sought external advice and expert input for the draft CCL 3. In addition to their own recommendations, the NRC and NDWAC recommended that the Agency seek opportunities to incorporate additional expert input in the development of the draft CCL 3. EPA convened several external expert panels at integral stages during the development of the draft CCL 3. EPA incorporated expert judgment and input from the scientific community into the CCL process for both chemicals and microbes. The Agency has requested a consultation with the Science Advisory Board that will take place in 2008.

For each expert panel, EPA sought panel members that provided a variety of disciplines and expertise. Panel members were encouraged to provide comments as individuals based upon their expertise and background, not as representatives of their respective organizational affiliations. Expert panel members were also encouraged to present individual comments if consensus comments were not developed. Separate panels were convened to review the draft chemical and microbial CCL 3 lists and the processes used to develop them. A more detailed discussion of the chemical and microbial expert review and input is provided in the support documents in the EPA Water Docket. A brief overview of the chemical and microbial expert review and stakeholder involvement follows.

a. Chemical Expert Input Panels

In September of 2006, EPA formed two external expert panels to provide specific input into the chemical CCL 3 process. In the first panel, experts reviewed the data sources and the process used to identify the chemical universe. EPA convened the second panel for a 3-day workshop to review the data and information used to develop screening criteria, the data and methodology for the classification approach, and to provide overall input into the CCL process. In summary, the panels recommended that EPA consider additional data sources in the process. They also commented on ways to improve and clarify the presentation of EPA efforts, thereby ensuring that the CCL 3 process for chemicals is more transparent. The expert panel reviewing the classification approach identified additional analyses and approaches to train and validate the models. The panel specifically commented on the varied nature of data elements and sources considered in the classification process. The panel recommended that to account for these varied data sources, contaminants be flagged based upon data certainty, and that uncertainty be considered in making a listing decision. The Agency applied their recommendations in the development of the draft CCL 3. In addition, the expert panels acknowledged the Agency's efforts to transparently present a complex process and noted that many of the questions posed by the panels were previously considered by EPA. They recommended that additional discussion and information in the support documents would add to the clarity of the process.

In March 2007, EPA convened a panel to review the preliminary draft CCL 3 list for the chemical contaminants in a two-day workshop. Panelists provided comments on a preliminary draft list of contaminants after receiving supporting materials and presentations from EPA staff. The panel's review focused mainly on the chemicals on the draft CCL 3. They provided comments on contaminants considered for the draft CCL 3 and commented on the supporting data and methods EPA used to identify the contaminants selected. They also provided general comments on the classification model output and the processes used to select chemical contaminants for CCL 3. In addition, they recommended EPA consider a strong outreach process to highlight the significant modeling and decision making processes used in its development.

The panel recognized the level of effort and detail that went into the development of the modeling process used to create the draft list and complimented EPA on these efforts. Comments from all the panels were considered by EPA and appropriate changes were incorporated into the process/protocols to formulate the draft CCL 3. (Specific recommendations and comments are further described in USEPA, 2008h.)

b. Microbial Expert Input Panels

EPA convened three workshops to review, discuss, and comment on the microbes considered and selected for ~~the draft CCL 3. In December~~ 2005, ~~a~~ group of expert microbiologists reviewed and commented on the universe of human pathogens and the screening criteria used to develop the PCCL. This panel agreed that focusing on human pathogens is a reasonable and pragmatic way to identify potential drinking water contaminants. While the panel suggested that animal pathogens may develop the ability to infect humans, they noted that these emerging contaminants should not be listed on the CCL based on the theoretical potential to become zoonotic pathogens. They also identified additional criteria and methods to apply those criteria to the Microbial Universe, which EPA incorporated into the CCL process.

In June 2006, a panel of experts met for three days to review EPA's implementation of recommendations by NRC and NDWAC to select microbes for the CCL. EPA implemented the NDWAC recommendation to develop a process that paralleled the chemical process yet still accounted for the different types of data and information that are uniquely available for microbial contaminants. Panel members agreed that health effects and occurrence of microbes should be evaluated to identify pathogens of the greatest health importance. The panel recommended that EPA use a decision tree approach for microbes rather than the classification approach suggested by NRC and NDWAC.

The panel further recommended that the Agency consider a different selection process than the one used for chemical contaminants, related to the different information available for microbes. Based on this recommendation, the Agency evaluated options to consolidate the potency and severity attributes for microbes into a single health effect attribute, developed a waterborne disease outbreak protocol, and considered occurrence as a single attribute. The Agency considered these and other recommendations as it developed the current three attribute selection process discussed in Section III.B. The panel also recommended that the Agency consider drinking water treatment and removing microbes from further consideration if conventional drinking water treatment protects public health. The Agency's considerations of these and other recommendations are discussed in the Microbial Expert Review support document (USEPA, 2008i).

In March 2007, EPA convened a third workshop to review the preliminary draft CCL 3 list of microbial contaminants. EPA provided the panel with background materials and staff presentations. The panel's review focused mainly on the draft CCL 3 for microbes. The panel also provided comments on the processes used to select the microbial contaminants. Panel members commented on specific microbes considered for the draft CCL 3 and commented on the data and processes EPA used to identify the contaminants selected. The panel noted that the Agency considered a comprehensive list of microbes and thought the draft CCL 3 was reasonable. The panel also recommended that the Agency consider adding a frequency of disease parameter to the health effects scoring protocol for future CCLs. For example, while the panel agreed with EPA that the health effects for *Naegleria fowleri* are severe, the health effects scoring protocol should consider the limited occurrence of disease. The panel also noted that this would help balance the consideration of less severe adverse health effects such as gastrointestinal illness that are more prevalent with consideration of more severe responses that are less prevalent, such as *N. fowleri*. The panel recommended that EPA provide further discussion of the rationale to evaluate waterborne disease and health effects equally in the protocol. The discussion of the Agency's rationale is included in Section III.B and addresses the importance of documented waterborne disease outbreaks to identify potential microbial contaminants for the CCL. (A more detailed summary of the expert comments is provided in USEPA, 2008 i.)

3. How are the CCL and UCMR Interrelated for Specific Chemicals and Groups?

EPA promulgated UCMR 2 on January 4, 2007 (72 FR 367 (USEPA, 2007 a; see also USEPA, 2007 b and c)). The UCMR program was developed in coordination with the CCL. Both programs consider the adverse health effects a contaminant may pose through drinking water exposures. Sixteen contaminants on the UCMR 2 monitoring list are also on the draft CCL 3. The draft CCL 3 includes acetochlor and its degradates, alachlor degradates, dimethoate, 1,3-dinitrobenzene, metolachlor and its degradates, RDX, terbufos sulfone, and four of the nitrosamines. In addition to the health effects data and potential occurrence, the UCMR 2 also considers analytical methods, availability of analytical standards, and laboratory capacity to conduct a nationwide monitoring program in selecting contaminants. The UCMR 2 includes nine contaminants that are not on draft CCL 3. The five polybrominated flame retardants can be measured by the same analytical method used for terbufos sulfone. The polybrominated flame retardants lacked sufficient occurrence information to be listed on draft CCL 3 (USEPA 2008 b). The polybrominated flame retardants are listed on UCMR2 because of recent concern that these have become more widespread environmental contaminants (e.g., Darnerud *et al.*, 2001) and this monitoring data will provide information for future CCLs. Similarly, 2,4,6-trinitrotoluene (TNT) and two of the nitrosamines also use an analytical method in the UCMR 2. The Agency will also use the results from UCMR 2 as a source of occurrence information during the selection of CCL 4, as well as for CCL 3 regulatory determinations. Alachor was listed on UCMR 2, but was removed from consideration for CCL 3 because there is an existing MCL.

IV. Request for Comment

The purpose of this notice is to present the draft CCL 3 and seek comment on various aspects of its development. The Agency requests comment on the approach used to develop the draft CCL 3 and also requests comments on the contaminants selected, including any supporting data that can be utilized in developing the final CCL 3. A number of contaminants considered for the draft CCL 3 may be of particular current interest. The following sections provide information for a few of the contaminants that are of most interest. Data obtained and evaluated for developing the draft CCL 3 and referred to in the following sections may be found in the docket for this notice. Specifically, the Agency is also asking for public comments on pharmaceuticals and perfluorinated compounds to identify any additional data and information on their concentrations in finished or ambient water and requests comment on how they have been considered in the CCL 3 process. The Agency is also seeking additional data and information on the occurrence and health effects of *H. pylori* and how this pathogen was considered in the CCL 3 process. Information and comments submitted will be considered in determining the final CCL 3, as well as in the development of future CCLs and in the Agency's efforts to set drinking water priorities in the future.

A. Pharmaceuticals

The Agency evaluated data sources to identify pharmaceuticals and personal care products that have the potential to occur in PWSs. The primary source of health effects information on ~~pharmaceuticals in the universe was the~~ Food and Drug Administration Database on Maximum Recommended Daily Doses (MRDD). This database includes the recommended adult doses for over 1,200 pharmaceutical agents. Occurrence information from USGS Toxics Substances Hydrology program's National Reconnaissance of Emerging Contaminants, and related efforts, provided ambient water concentration data for 123 contaminants, which include pharmaceuticals. Other data sources included TRI and high production volume chemical data. From this analysis, EPA included 287 pharmaceuticals in the Chemical Universe. These pharmaceuticals had maximum recommended daily dose information that EPA used to evaluate adverse health effects. EPA considered those pharmaceuticals for which MRDD values and occurrence information were available and pharmaceuticals that were in Toxicity Category 1, using the same criteria discussed in Section III.A.2.a. EPA found that less than two percent of the pharmaceuticals included in the MRDD database fell into this category.

EPA applied the LOAEL screening protocols to contaminants with MRDD values. The LOAEL protocol was used because pharmaceutical agents, although used for their beneficial effects, have associated side-effects that may be adverse. Chemicals evaluated with these data had similar modal values and distributions to the toxicity values from IRIS. The range of toxicity values in this database covered 9 orders of magnitude when evaluated based on their rounded logs. They had the same modal value as the LOAELs from IRIS and a very similar distribution. Thirty-five percent of the IRIS LOAELS and 38 percent of the MRDDs had the modal rounded log. Thirty-three percent of the LOAELs and 19 percent MRDDs had rounded logs that were lower than the mode, while 31 percent of the LOAELs and 44% of the MRDDs had rounded logs that were above the modal log value.

The screening process moved approximately 10 percent of the pharmaceuticals in the Universe to the PCCL. All toxicity data on those chemicals were included in the screening with the most serious qualitative or quantitative measure of toxicity determining placement in a toxicity category. Only one of the PCCL chemicals (diazinon, a veterinary product as well as a pesticide) had water concentration data. Two other pharmaceuticals: phenytoin (an anticonvulsant) and nitroglycerin (treatment of angina), had release data. The remainder were scored for ~~occurrence based on production~~ information, which meant that they fell into the low certainty bin for their occurrence parameters. Nitroglycerin is the only pharmaceutical that is included on the draft CCL 3. EPA is aware of concerns regarding the potential presence of pharmaceuticals in water supplies. The Agency is seeking additional data and information on the concentrations of pharmaceuticals in finished or ambient water and requests comment on how pharmaceuticals have been considered in the CCL 3 process.

B. Perfluorooctanoic Acid and Perfluorooctane Sulfonic Acid

EPA evaluated perfluorinated compounds in the CCL 3 process and requests comment on its decisions to include perfluorooctanoic acid (PFOA) and not to include perfluorooctane sulfonic acid (PFOS) on the draft CCL 3. EPA identified potential health effects and occurrence information for these compounds from the data sources discussed in Section III. The data used for these compounds are discussed in the support documents in more detail. Available analytic methods for these chemicals limited the occurrence data for these compounds. The Agency identified data on the annual production from CUS/IUR indicating limited production and possible release to the environment. Several organizations nominated PFOS and PFOA for consideration in the CCL process. The nominations noted that these chemicals are persistent in the environment and have been detected at varying levels in drinking water and ambient water in smaller specialized studies. EPA collected the information cited in the nominations and evaluated each of these chemicals. The Agency included PFOA on the draft CCL 3 because it met the criteria for inclusion on draft CCL 3 based on drinking water occurrence studies in Ohio and West Virginia (Emmett, *et al.*, 2006) and on health effects data indicated through animal studies (USEPA, 2005 a).

The Agency did not include PFOS on the draft CCL 3. Occurrence data for PFOS characterized detections in several States (Boulanger, *et al.*, 2004, Hansen, *et al.*, 2002, Goeden and Kelly, 2006). These data showed that levels of detection for PFOS in ambient water ranged from 20 to approximately 100 parts per trillion. Data identified in the nominations process detected PFOS at higher concentrations in areas surrounding landfills known to be contaminated with industrial waste containing PFOS. The CCL process did not consider occurrence data from targeted studies of contaminated waste sites, however. Such studies are usually developed to identify and characterize hazardous waste cleanup efforts and may not be representative of occurrence in drinking water not in close proximity to the study site. PFOS was phased out of production in the U.S. between 2000 and 2002, and regulation limits its importation to a very small number of controlled, very low release uses, (67 FR 72854; December 9, 2002 (USEPA, 2002 c)). Based on the general absence of occurrence data, combined with the phase out, effectively eliminating most future releases, PFOS did not meet the criteria for CCL 3.

The Agency is evaluating data related to PFOA in a formal risk assessment process under the Toxic Substance Control Act. EPA's Science Advisory Board (SAB) completed a review of a draft risk assessment in 2006 and SAB made recommendations for the further development of the risk assessment. A final risk assessment may not be completed for several years, as a number of important studies are underway. The Agency is also participating in additional research regarding the toxicity and persistence of related perfluorochemicals, as well as research to help identify where these chemicals are coming from and how people may be exposed to them.

C. Helicobacter pylori

Helicobacter pylori is a pathogen that causes gastric cancer in addition to acute gastric ulcers. EPA placed this pathogen on the draft CCL. However, the analysis for *H. pylori* differs from the other pathogens due to the long term and/or chronic nature of its health effects rather than the more common acute effects of most waterborne pathogens. This organism is an emerging pathogen whose impact has only recently begun to be understood. Given the slow development of adverse health effects due to infection by *H. pylori*, it is more difficult to link contamination of drinking water and show a waterborne disease outbreak. Therefore, given the long timeframe of cancer and ulcer development (as opposed to the commonly acute gastrointestinal illness of nearly all the other pathogens on the PCCL) as well as the ongoing nature of the research, EPA used peer-reviewed scientific papers to score the health effects of *Helicobacter pylori*. EPA request comment on the process of selection of microbial contaminants that cause chronic rather than acute health effects.

V. EPA's Next Steps

Between now and the publication of the final CCL, the Agency will evaluate comments received during the comment period for this notice, consult with the SAB, and re-evaluate the criteria used to develop the draft CCL and revise the CCL, as appropriate.

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Dated: February 6, 2008.

Benjamin H. Grumbles,

Assistant Administrator, Office of Water.

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Toxaphene Risk Assessment:
Re-evaluation and Data Development

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August 21, 2007

10504988

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Presentation Outline

- Chronology of risk assessment and regulation of toxaphene
- Data development needs

2004-2005

- Reviewed the relevant toxicology data on technical and weathered toxaphene
- Considered relevant toxicology issues that might affect the toxaphene risk assessment based on technical toxaphene and weathered toxaphene
  - Existing EPA risk assessment
  - Goodman et al. 2000
  - European risk assessment for fish (MATT)
  - EPA Region 4 risk assessment position
  - Simon and Manning on risk assessment of the 3 persistent congeners
- Finalized ability to run ECD-NCI-MS at the Hercules Research Center
- Met with EPA Region 4 about current views on toxaphene risk assessment methodology

2006

Developed data Used in MATT Study in-vivo on rats

- Worked with Dr. Brouwer and Dr. Besselink on their model for tumor promotion assays for weathered toxaphene, which have been accepted by the EU for human risk assessment of toxaphene residues in fish (MATT Report)
- Reviewed EPA OIG report on toxaphene risk assessment for landfill clean-up
- Presented information on toxaphene analysis to EPA Region 4 and to EPA OIG in response to the Inspector General's reports related to 009 landfill site

2007

believe sensible approach, but should be supported by mice not rats. *European source of toxaphene may be different.

- Developed a toxicology research plan to improve the data to be used in support of the risk assessment proposals by the EU (MATT) and by Simon and Manning (3 persistent congeners) instead of rats
  - Mouse liver tumors as the critical effect or point of departure for risk assessment
  - Weathered toxaphene toxicology data need to be further developed to build on existing data for risk assessment

Current Activities

- Created an independent Scientific Advisory Panel (SAP) to review and comment on the proposed testing plans for an improved risk assessment
  - Dr. Abraham Brouwer, Biodetection Systems, B.V.
  - Dr. Jay Goodman, Michigan State University
  - Dr. James Klaunig, Indiana University
  - Dr. E.E. McConnell, ToxPath
  - Dr. Richard Reiss, Exponent
  - Dr. Ted Simon, Consultant
- Incorporated the SAP comments into the testing plan
- Initiated discussions with several laboratories that can do the in vitro work
- Working to expedite the in vivo study design and laboratory selection, so those studies can begin as soon as the in vitro data are available

Phenobarbital — Hex SED HEP SED — may not be able to have enough to run in vivo

Research Program Status

- In vitro studies have been designed and a laboratory is being selected
- In vivo studies will be conducted after the in vitro work
- In vivo data should be applicable to the risk assessment of weathered toxaphene based upon the concentrations of the 3 persistent congeners

In Vitro Study Design

- Mouse liver cells as the target
- Gap junction intercellular communication (GJIC) as the endpoint predicting liver tumor promotion
- Test will include:
  - Negative control (vehicle)
  - Phenobarbital (positive control)
  - Technical toxaphene
  - P26, P50, P62, HxSed, HpSed and mixtures to model weathered toxaphene

In Vivo Study Design

- Mouse as the test species
- Initiate with diethylnitrosamine
- Promotion tested for by measuring GJIC in vivo after treatment with:
  - Phenobarbital
  - Technical toxaphene (diet and gavage comparison)
  - P26, P50 and P62 (gavage) for weathered toxaphene model
  - Other congeners or mixtures based on in vitro data
- The design of this study will be modified depending upon the data developed in vitro

2 years to get enough congeners for study

Conclusions

- The study is designed to test the same species that showed liver tumors for technical toxaphene, the mouse
- The congeners were proposed by Simon and Manning and by the OIG and should represent the congeners of concern in weathered toxaphene
- Limiting factor is the availability of congeners
- Laboratory selection is currently underway and the protocol will be final after selection

Conclusions - 2

- The data should provide a basis to compare the in vivo gavage data on the congeners representing weathered toxaphene to technical toxaphene potency by gavage and by dietary exposure
- The dietary study relates back to the NCI studies on technical toxaphene
- Ultimately this will allow a dietary relative potency to be established for risk assessment of weathered toxaphene

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Development of a reference dose for the persistent congeners of weathered toxaphene based on in vivo and in vitro effects related to tumor promotion

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Abstract

Toxaphene is a mixture of chlorinated camphenes and bornanes that was produced and used in the United States until 1982. 1.3 million tons of toxaphene have been released worldwide. "Technical" toxaphene (TT) consists of a mixture of up to 800 different chemicals, known as congeners. TT weathers in the environment by both biotic and abiotic processes. The human body burden of toxaphene consists of only five persistent congeners that are not metabolized; three of these occur in considerably greater amounts than the other two. Because of the rapid metabolism and excretion of the non-persistent congeners, the persistent congeners that make up the human body burden most likely play a role in eliciting any potential adverse effects. EPA's toxicity assessment for TT is based on the occurrence of ~~liver cancer in rodents, and considerable doubt exists whether this assessment is applicable to weathered toxaphene (WT). Using exper~~imental results from European Union scientists, a reference dose (RfD) was developed for WT based on the three most persistent congeners that comprise the human body burden. The critical effect chosen was tumor promotion and this endpoint is considered protective for other endpoints as well. Although RfDs are typically derived for non-carcinogenic effects, the endpoint of tumor promotion is appropriate for RfD development because the experimental data suggest a dose threshold. The RfD for weathered toxaphene represented by the sum of the three major persistent congeners ($\sum$3PC) is 2E−05 mg/kg-day. To apply this reference dose to a particular WT mixture, information is needed regarding the percentage of $\sum$3PC in the mixture.
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Keywords: Toxaphene; Weathering; Organochlorine; Pesticide; Tumor promotion; Reference dose

1. Introduction

Toxaphene is a mixture of chlorinated camphenes and bornanes that was produced and used in the United States until 1982. Toxaphene has the distinction of being the most used pesticide in history with 1.3 million tons having been released worldwide. Technical toxaphene (TT) consists of a mixture of up to 800 different chemicals, known as congeners. Once in the environment, TT undergoes weathering by both biotic and abiotic processes and the number and identity of the congeners in weathered toxaphene (WT) are different than those in TT. Hence, toxaphene has presented a significant challenge to analytical chemists (de Geus et al., 1999, 2000). In addition, WT appears to have toxicity characteristics that are different from TT.

There is a large and growing literature on the analysis, occurrence, and toxicity of WT (e.g., de Geus et al., 1999, 2000) Several nomenclature systems have evolved. Readers unfamiliar with toxaphene chemistry invariably find multiple names for the same chemical to be a confusing issue. Regarding human exposure to WT, there are three significant congeners. The structures and names of these three congeners are shown in Table 1. Enantiomeric chiral forms exist for many of the congeners. Some

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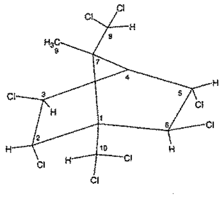
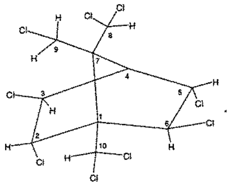
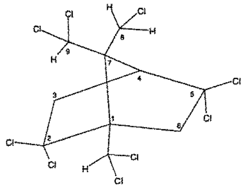
Table 1
Nomenclature and structure of the three persistent toxaphene congeners

Parlar name	Andrews–Vetter code	Wester code	IUPAC names of both chiral forms	Structure
p-26	B8-1413	B[12012]-[202]r B[12012]-[202]s	2-endo, 3-exo, 5-endo, 6-exo, 8,8,10,10 octachlorobornane or 2-exo, 3-endo, 5-exo, 6-endo, 8,8,10,10 octachlorobornane	
p-50	B9-1679	B[12012]-[212]r B[12012]-[212]s	2-endo, 3-exo, 5-endo, 6-exo, 8,8,9,10,10 nonachlorobornane or 2-exo, 3-endo, 5-exo, 6-endo, 8,8,9,10,10 nonachlorobornane	
p-62	B9-1025		2,2,5,5,8,9,9,10,10 nonachlorobornane	

individual toxaphene congeners are also known as "Parlars" after Dr. H. Parlar, a pioneer of toxaphene analytical chemistry (e.g., Gill et al., 1996). Specific congeners have been given a Parlar number to easily refer to them (e.g., Parlar-26 or p-26). The major toxaphene congeners that persist in fish, marine mammals, human serum, and human breast milk are p-26, p-50, and p-62 (Table 1). The congeners p-23, p-40, p-41, and p-44 are also observed in lower amounts.

Regarding terminology in this paper, TT refers to the original technical toxaphene mixture;. WT refers to the entire set of congeners remaining after TT has weathered in the environment; and, as defined in this paper, $\sum$3PC refers to the sum of the concentrations of p-26, p-50, and p-62 occurring in either TT or WT.

1.1. Cancer slope factors for technical toxaphene

In 1991, EPA's IRIS program developed a cancer slope factor (CSF) for TT based on two rodent studies, the 1978 Litton Bionetics B6C3F1 mouse study and the 1979 NCI Osbourne-Mendel rat study that both administered technical toxaphene via feeding. The slope factor was derived using the linearized multistage model and had a value of 1.1 per mg/kg-day (e.g., Crump, 1984). In 2000, a peer review panel reevaluated the CSF for TT and recommended that the value be reduced to 0.1 per mg/kg-day (Goodman et al., 2000). The basis of this recommendation was a reexamination of the original histological materials by an expert pathology working group and application of benchmark dose modeling to account for high background liver tumor rates. In 2003, CAL-EPA (OEHHA, 2003) determined a CSF for TT based on the NCI and Litton Bionetics rodent studies. The value of the slope factor was 1.2 per mg/kg-day, essentially the same as the 1991 EPA slope factor. In 2004, Buranatrevedh (2004) derived a CSF of 0.86 per mg/kg-day from the original rodent data, also a similar value.

The major and insurmountable difficulty with all of these derivations is that all are based on application of TT to rodents and may not be appropriate for evaluating the potential toxicity of WT to humans.

1.2. Weathering of toxaphene

Toxaphene weathers in different ways in different environmental settings to produce different congener mixtures (Ruppe et al., 2003, 2004). In addition, different animals metabolize various toxaphene congeners to varying degrees (Angerhofer et al., 1999) and different species of animals end up with different toxaphene congener profiles comprising their respective body burdens. Both transformation of toxaphene mixtures by bacterial action in sediments or soils and metabolism in animals are considered forms of "weathering."

In animals, including human beings, differences in body burden are due to differences in the extent that individual congeners are metabolized and excreted. The major toxaphene congeners that persist in fish, marine mammals, human serum and human breast milk are p-26, p-40/41, p-44, p-50, and p-62. Barr et al. (2004) reported concentrations of toxaphene congeners from pooled human serum from three US cities. Only p-26 and p-50 were positively identified in the serum samples. There were indications that p-40/41, p-44, and p-62 were also present. Gill et al. (1996) presented methods for toxaphene congener analysis in serum and observed p-26, p-40/41, p-44, and p-50 in human serum extracts. Bjerregaard et al. (2001) measured toxaphene congeners in plasma of Inuit men and women in Greenland and found detectable levels of p-26, p-50, and p-62. Polder et al. (2003) measured p-26, p-50, and p-62 in human breast milk samples from Kargopol, Severodvinsk, Arkhangelsk, and Naryan-Mar, Russian towns all north of 60° latitude. Skopp et al. (2002b) measured p-26, p-41, p-44, and p-50 in human breast milk obtained from mothers in the north Rhine area of Germany. Sandanger et al. (2003) measured organochlorines in the plasma of delivering mothers in northern Russia and found detectable concentrations of p-26 and p-50; p-32, p-38, p-40, p-42, p-44, p-51, p-58, p-62, and p-69 were not detected. Walker et al. (2003) found detectable concentrations of p-26 and p-50 in maternal and umbilical cord blood plasma from mothers and newborns in northern Canada; p-32, p-62, and p-69 were analyzed but not detected. Average percentages of the congeners in the human body burden were calculated based on these five sources and are shown in Table 2. These three congeners, p-26, p-50, and p-62, comprise about 90% of the average human body burden.

Table 2
Toxaphene congeners and their average percentages in the human body burden from Gill et al. (1996), Polder et al. (2003), Skopp et al. (2002b), Sandanger et al. (2003), Walker et al. (2003)

Congener	p-26	p-40/41	p-44	p-50	p-62
Percent in human body burden	32.8%	2.7%	3.5%	54.7%	6.3%

Metabolism and excretion of toxaphene occurs relatively rapidly in biological systems. These processes are also considered a form of "weathering." Oral administration of toxaphene to mammals and birds results in fecal passage of about 40% of the administered chemical and metabolism and urinary excretion of the remaining toxaphene on a time scale of weeks (Andrews et al., 1996; Biessman et al., 1983; Pollock and Hillstrand, 1982; Pollock and Kilgore, 1980; Mohammed et al., 1983). Only five or six persistent congeners remain in the tissues of mammals and birds. Because of this rapid "weathering," the exposure of higher animals to TT or WT is essentially equivalent to $\sum$3PC exposure, and any toxic effects are very likely due to $\sum$3PC.

1.3. Evaluation of risk of tumor promotion using a reference dose and threshold approach

EPA recently released the cancer guidelines (USEPA, 2005). The greatest emphasis in these guidelines is placed on understanding the mode of action of potential carcinogens and taking the mode of action into account when developing a toxicity criterion. The guidelines include the possibility that nonlinear threshold models of cancer will be considered as the basis of regulatory toxicity criteria. Ideally, for threshold carcinogens, sufficient data above and below the dose threshold would exist to perform dose response modeling (USEPA, 2000); in cases where such modeling is not feasible, it is appropriate to use the reference dose approach for evaluation of cancer-associated chemical such as a tumor promoter that exhibits a dose threshold.

The reference dose (RfD) derived here is based on a no-observed-adverse-effect-level (NOAEL) from an in vivo study in rats administered WT via weekly subcutaneous injection (Besselink et al., 2000; MATT, 2000). WT was produced by "weathering" technical toxaphene for 2 months in farmed codfish. Cod liver extract (CLE) was then used as a source of WT. Concentrations of the three persistent congeners in CLE were available for all doses (Besselink et al., 2000; MATT, 2000). The critical effect was the occurrence of altered hepatic foci (AHF) expressing placental glutathione-*S*-transferase (GSTp-AHF). These foci are as an indication of tumor promotion (Ito et al., 1989; Krutovskikh et al., 1991). Additional mechanistic support for endpoint of tumor promotion is provided by an in vitro study of the disruption of gap junctional intercellular communication in the Hepa1c1c7 mouse liver cell line from exposure to WT (Besselink et al., 2000; MATT, 2000).

Because the RfD derived here is based on the toxicity of the three persistent congeners, p-26, p-50, and p-62, it is not directly comparable with other toxicity criteria for TT and WT. EPA's cancer slope factor for technical toxaphene has different units than the RfD. The tolerable daily intake (TDI) for WT derived in MATT (2000) is based on the entire WT mixture and the percentage of $\sum$3PC may be different in different WT mixtures.

1.4. Applying the RfD to obtain a cleanup level

If the percentage of $\sum$3PC in a WT mixture is known, then cleanup levels may be expressed either in terms of $\sum$3PC or in terms of WT by back calculation to the appropriate WT concentration based on the percentage of $\sum$3PC in the mixture. Cleanup levels based the RfD for $\sum$3PC may need to be expressed in terms of WT for comparison with cleanup levels based on other toxaphene toxicity criteria. A numerical comparison and sample calculations are provided in Section 4. In addition, the analytical methods used need to be considered; different methods give different analytical results (de Geus et al., 2000)

2. Derivation of a reference dose for tumor promotion based on appearance of GSTp-AHF in rat liver

The sole set of toxicity studies that used WT and measured $\sum$3PC in the WT mixture was conducted as part of the European effort, "Investigation into the Monitoring, Analysis, and ~~Toxicity of Toxaphene." (MATT, 2000)~~. These toxicity studies were also published separately (Besselink et al., 2000). Here, we use the results of these toxicity studies to derive an RfD for $\sum$3PC.

The standard methods for developing reference doses have been published elsewhere and are well known (Barnes and Dourson, 1988). A three-step process for the derivation of an RfD was followed: (1) choice of a critical effect for $\sum$3PC; (2) derivation of NOAELs for $\sum$3PC from the in vivo study in the MATT (2000); (3) choice and application of appropriate uncertainty factors.

2.1. Critical effect of $\sum$3PC

Based on the early rodent studies, the critical effect for TT was liver cancer (e.g., Goodman et al., 2000). Three possibilities for the critical effect of $\sum$3PC are considered: (1) $\sum$3PC acts as a genotoxic carcinogen; (2) $\sum$3PC acts as a developmental toxicant; (3) $\sum$3PC acts as a carcinogen via tumor promotion. If $\sum$3PC acts as a genotoxic carcinogen, then derivation of a cancer slope factor rather than a reference dose would be appropriate. If $\sum$3PC acts as either a developmental toxicant or a tumor promoter and if these effects have dose thresholds, then derivation of a reference dose is appropriate.

Recently, EPA has begun an effort to "harmonize" cancer and non-cancer risk assessment (USEPA, 1997b, 1998). The use of an RfD for tumor promotion is consistent with this "harmonization" effort. Colloquia held regarding the framework for human health risk assessment included harmonization of cancer and non-cancer endpoints. These colloquia stressed that understanding the mode of action of a particular effect was key in understanding toxicity and arriving at a meaningful regulatory toxicity criterion. The development of an RfD for the tumor promoting effect of the persistent congeners of toxaphene that comprise the human body burden is consistent with this effort to harmonize cancer and noncancer risk assessment, and, as already discussed, also consistent with EPA's cancer guidelines (USEPA, 2005).

It is appropriate to consider studies on the toxicity of TT when considering WT because the ultimate toxicants are the persistent congeners, present in both TT and WT. In fact, consideration of the toxicity of TT in a risk assessment for $\sum$3PC is similar to the practices in EPA's pesticide program. In that program, because many pesticides produce their effects through metabolites, the pesticides can be administered in animal studies to ascertain the toxic effect of the metabolites, so called "auto-testing."

What follows is a discussion of the likelihood and possible thresholds of these three possible effects of WT and the rationale for choosing tumor promotion as the critical effect.

2.1.1. Genotoxicity of TT or WT

In some studies with prokaryotic systems, TT has been shown to be mutagenic in the Ames test and others. Both TT and WT have been shown to be mutagenic in the Ames ~~test (Young and Freeman, 2001, 2004), but the mutagenic~~ity of WT appears less than that of TT (Steinberg et al., 1998). Bartos et al. (2005) showed both TT and WT to be genotoxic in some bacterial systems, but activation of TT by human microsomal preparations produced a negative result in the Ames test with salmonella TA 98 and TA 100, which contain the pKm101 plasmid. In other work, activation of TT by rat S9 liver fraction produced a positive Ames test in these strains (Hooper et al., 1979; Mortelsman et al., 1986).

In eukaryotic systems, the picture is even less clear. Mutagenicity of TT could not be shown in the mouse dominant lethal assay (NTP, 1979). In studies of sister chromatid exchange in Chinese hamster lung cells and human lymphocyte cultures, TT produced a weak response that was reduced by metabolic activation (Sobti et al., 1983; Steinel et al., 1990). Toxaphene was clearly not a mutagen in the mouse dominant lethal assay (Epstein et al., 1972). Boon et al. (1998) observed genotoxicity for TT as well as four toxaphene congeners (p-26, p-32, p-50, and p-62) in the Mutatox assay. Addition of rat S9 fraction or microsomes of harbour seal or albatross decreased the genotoxic potential of single congeners and TT. This indicates that organisms with a lower capacity to metabolize toxaphene might be more susceptible to the mutagenic effects of TT than organisms with a greater metabolic capacity.

In humans, EPA did not observe leukocyte chromosomal aberrations in agricultural workers using toxaphene

(USEPA, 1978). However, an accidental exposure of eight women to airborne toxaphene resulted in an increase in chromosomal aberrations (Samosh, 1974).

There is certainly no clear and convincing evidence that TT or WT are genotoxic in humans and the critical effect of cancer via a genotoxic mechanism was not considered further.

2.1.2. Developmental effects of toxaphene

Calciu et al. (1997) investigated the effects of TT, p-26, p-50 and an equimolar mixture of p-26/p-50 on the development of cultured rat embryos. The concentrations used were 100, 1000 and 5000 ng/ml. All treatments caused growth retardation of the embryos at all doses. These authors suggest that levels of toxaphene in umbilical cord blood estimated from measured levels in breast milk of Inuit women are 1/1000 of the lowest concentrations used in the experiment.

Calciu et al. (2002) discovered an interaction between TT, p-26, and p-50, on one hand, and hyperglycemia, on the other hand, that affected the development of cultured rat embryos. The dose range was 100, 1000, and 5000 ng/ml. Again, the levels of toxaphene or individual congeners used appear to be at least 1000 times greater than the levels of toxaphene predicted in cord blood based on plasma levels in Inuit women (Bjerregaard et al., 2001) and Calciu et al. (2002) concluded that observing effects in humans would be unlikely. Thus, while both TT and WT may produce developmental toxicity, it appears that the concentrations required to do so are much higher than body burden concentrations in a highly exposed human population.

Because TT and the two congeners were added directly to the culture medium containing the rat embryos, it is impossible from this in vitro experiment to determine an estimate of the dose that would be associated with human developmental effects. Nonetheless, a LOEC (Lowest Observed Effective Concentration) of 100 ng/ml or 100 μg/L can be established for TT, p-26, and p-50 from this study.

2.1.3. Toxaphene as a tumor promoter

Inhibition of gap junctional intercellular communication (GJIC) has been postulated to release initiated cells from suppressing effects of signals passing from surrounding cells (Kao et al., 1995; Yamasaki, 1990). Disruption of gap junctional communication can be measured by intercellular transfer of the dye Lucifer yellow following application of the tumor promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA) (McKarns and Doolittle, 1982). A study by Kang et al. (1996) showed that noncytotoxic concentrations of TT inhibited GJIC in normal human breast epithelial cells in a dose-dependent way after 90 min of exposure.

The appearance of GSTp-AHF is associated with a decrease in GJIC with surrounding cells and eventual progress to cancer (Ito et al., 1989; Krutovskikh et al., 1991). This effect appears to be due to reduced expression of connexins, the gap junction forming protein (Fitzgerald et al., 1989). However, the association is not complete and disruption of gap junctions and down-regulation of connexins, on one hand, and the expression of GSTp, on the other hand, may represent two distinct pathways to tumor formation (Bager et al., 1997). Toxaphene and other nongenotoxic carcinogens have been shown to disrupt GJIC (Kang et al., 1996; Kolaja et al., 2000).

Based on these earlier studies, Besselink et al. (2000) investigated the tumor promoting effects of WT using both in vivo and in vitro assays. The cod liver extract used in the MATT study clearly disrupted gap junctions in mouse Hepalclc7 cells at all concentrations tested (Besselink et al., 2000) and tumor promotion is considered the most likely endpoint for WT.

2.2. Description of the study providing the critical effect

2.2.1. Preparation of weathered toxaphene mixture

Weathered toxaphene was prepared by dosing codfish with 30 ppm TT via feed pellets for two months. Cod liver extracts (CLE) were used as the source of weathered toxaphene. At the conclusion of the feeding period, a total of 1880 mg of toxaphene residue was obtained from the pooled cod livers (MATT, 2000). Analysis of the CLE revealed a mixture of many toxaphene congeners, including p-26, p-50, and p-62. As indicated, because of rapid metabolism and excretion of the non-persistent congeners, exposure of mammals to technical toxaphene or WT mixtures is essentially equivalent to exposure to $\sum$3PC, and any toxic effects are likely due to $\sum$3PC.

A chromatogram provided in the MATT report shows that the CLE was considerably enriched in p-26, p-32, p-50, and p-62. However, the mixture of toxaphene residues in CLE was complex and contained more individual congeners than weathered toxaphene obtained from other biotic sources (Chan et al., 1998; Chan and Yeboah, 2000; Skopp et al., 2002a; Maruya, 2000). Technical toxaphene was weathered in cod for two months only to produce CLE. The percentage of $\sum$3PC in CLE was between 0.2 and 0.3%, which was much lower than the percentage observed in WT from environmental sources (e.g., Tables 6 and 7) The low percentage of $\sum$3PC in CLE may be related to the short period of weathering.

2.2.2. In vivo study of tumor promotion

Female Sprague–Dawley rats in groups of three or four animals were given partial hepatectomies at the age of 6 weeks. Diethylnitrosamine (30 mg/kg) was given by intraperitoneal injection 24 h after hepatectomy. Beginning 5 weeks later and lasting for 20 weeks, the rats were then dosed weekly via subcutaneous injection with either technical toxaphene (TT), UV-treated toxaphene (UVT), cod liver extract (CLE) or dioxin (2,3.7.8-TCDD) in a corn oil vehicle. The lowest concentration of CLE in the in vivo study was 0.46 mg/ml corn oil and the highest concentration was 12.5 mg/ml corn oil. 1 ml of corn oil was administered subcutaneously per week. MATT (2000) indicates these dosing concentrations are expressed as UVT-equivalents whereas Besselink et al. (2000) report these numeric values only.

Presumably, because UV treatment is another means of weathering toxaphene, the doses in CLE were expressed as UVT equivalents, although both MATT (2000) and Besselink et al. (2000) failed to provide the details of this equivalence or the rationale for the UV treatment. Here, the concentrations of ∑3PC were used as the basis of the RfD dose because these are the predominant congeners in the human body burden. Concentrations of p-26, p-50, and p-62 in CLE were provided in MATT (2000) and the details of the UVT equivalence are not necessary.

A range of doses of TT, UVT, and CLE were given to the rats. A single dose of dioxin was given as a positive control. One week after the last dose, the rats were sacrificed and their livers obtained (Besselink et al., 2000; MATT, 2000).

The endpoint of the in vivo assay was the production of GSTp-AHF. Only TCDD produced positive foci. The lower three doses of CLE were not significantly different from the corn oil control in terms of the number of GSTp-AHF. The highest dose showed a decrease in GSTp-AHF, indicating some possible cytotoxic effect that may not be related to tumor promotion.

The ratios of the three persistent congeners in the doses used in the in vivo assay approximate those observed in biotic samples (Table 5). Hence, ∑3PC is approximately proportional to the dose of WT. The concentrations of the three persistent congeners in the rats' livers were measured at the end of the experiment. Only the highest dose (12.5 mg/kg-week) resulted in detectable liver concentrations with detections of 2 and 3 μg/kg wet weight for p-50 and p-62, respectively, and a nondetect analytical result for p-26 (Table 3).

Because of the difficulty of interpreting the in vivo results observed at the highest dose of CLE (12.5 mg/kg-week), the next highest dose was considered a NOAEL. At this next highest dose of 4.17 mg/kg-week as UVT equivalents, the number of GSTp-AHF was not significantly different from the number of GSTp-AHF in corn oil controls. This dose is equivalent to 0.0021 mg/kg-day of ∑3PC (Table 2). However, with this dose of 4.17 mg/kg-week CLE as UVT equivalents, concentrations of p-26, p-50, and p-62 in the rats' livers were below analytical detection limits (Table 3).

2.2.3. *In vitro study of gap junctional intercellular communication*

The in vitro study measured intracellular communication between mouse Hep1c1c7 cells in culture by observing the spread of Lucifer Yellow dye between adjacent cells. This dye has been used for a number of years to observe disruption of gap junctional communication and electrical junctions between nerve cells. (e.g., McKarns and Doolittle, 1982; Spencer and Satterlie, 1980). 2,3,7,8-TCDD was used as a positive control. A dose-dependent response was observed for CLE in this assay. The lowest concentration for CLE extract in the in vitro study was 1 mg/ml (Besselink et al., 2000). In the in vitro study, an effect was observed at 1 mg/ml—hence, this concentration represents

Table 3
Percentage of p-26, p-50, and p-62 in the MATT dosing vehicle and calculated doses of ∑3PC in the in vivo study

Concentration UV-T equivalents (mg/ml oil)	0.46	1.39	4.17	12.5
Concentration (μg/ml oil)				
p-26	0.3	1.2	3.4	9.9
p-50	0.4	2	5.5	16.8
p-62	0.4	2.1	6	17.5
∑3PC	1.1	5.3	14.9	44.1
Percentages of three congeners in CLE				
%p-26	0.065	0.086	0.082	0.079
%p-50	0.087	0.144	0.132	0.134
%p-62	0.087	0.151	0.144	0.140
∑3PC	0.239	0.381	0.357	0.354
Doses (mg/kg-day) used in the in vivo study				
CLE as UVT	0.066	0.198	0.60	1.79
p-26	4.28E–05	0.00017	0.00049	0.0014
p-50	5.71E–05	0.00029	0.00079	0.0024
p-62	5.71E–05	0.00030	0.00086	0.0025
∑3PC	1.57E–04	0.00076	**0.0021**	0.0063
Liver concentrations in the in vivo study (μg/kg)				
p-26	<0.4	<0.4	<0.5	<1.0
p-50	<0.5	<0.4	<0.5	2
p-62	<0.5	<0.5	<0.5	3
∑3PC	<1.4	<1.3	<1.5	5–6

The chosen NOAEL is in boldface and highlighted.

a LOEC for CLE. The corresponding LOEC for ∑3PC based on a concentration of CLE of 1 mg/ml would be 2.4 μg/ml because the percentage of ∑3PC in CLE at the lowest dosing concentration is 0.24% (Table 3).

Kang et al. (1996) used technical toxaphene in an in vitro assay of GJIC in normal human breast epithelial cells and observed a LOEC of 1.25 mg/ml. This result is not directly comparable to those from MATT (2000) because of three factors: (1) the differences between WT and TT; (2) the fact that the percentage of ∑3PC in TT used by Kang et al. (1996) is not known; and (3) an internal discrepancy in Kang et al. (1996) whether toxaphene concentrations were expressed in mg/ml or μg/ml.

2.3. Determination of a NOAEL for tumor promotion from the MATT study

Generally, it is preferable to develop a point of departure for an adverse effect using benchmark dose modeling (USEPA, 2000). These models use all the data from dose response studies instead of a NOAEL or LOAEL. However, in the in vivo study (Besselink et al., 2000; MATT, 2000), the doses were not high enough to observe a dose–response curve or even a LOAEL.

The doses of ∑3PC were recalculated based on the rats' initial average body weights and average weight gains given in Table 4 of chapter 5 of the MATT report. These doses are also shown in Table 3 of this paper.

As indicated, at the highest in vivo dose of 12.5 mg/kg-week CLE, there was a reduction in the number of GSTp-AHF in the rats' livers compared with the number in controls and the highest dose group result was not considered usable. No differences were observed in the number or size of GSTp-AHF foci at the three lower doses. The highest dose of these three (4.17 mg/kg-week CLE as UVT equivalents) was below the dose threshold for observing the critical effect. Hence, this dose of 4.17 mg/kg-week CLE or 0.002 mg/kg-day of ∑3PC can be considered a NOAEL (Table 3).

The rats' liver concentrations of p-26, p-50, and p-62 were measured at the conclusion of the study. This information was presented in MATT (2000) but not in Besselink et al. (2000). At the highest dose of 12.5 mg/kg-week of CLE, the concentration in the rats' livers of ∑3PC was less than 6 μg/kg wet weight (Table 3 in chapter 5 of MATT (2000) and Table 3 here). At lower doses, the concentrations of the three persistent congeners were below analytical detection limits.

To compare the internal liver concentration of ∑3PC in the in vivo study with the LOEC from the in vitro study, one can multiply the percentage of ∑3PC and the CLE concentration. The in vitro LOEC for CLE was 1 mg/ml (Besselink et al., 2000). The percentage of ∑3PC in CLE at this lowest dose level was 0.24%. Hence, assuming the intact rat liver cells are similarly susceptible to interruption of GJIC as the Hep1c1c7 cells, the potentially effective concentration of ∑3PC in the rats' livers would be 0.24% of the in vitro LOEC of 1 mg/ml or 2.4 μg/ml of ∑3PC. Expressing this value in the same units as ∑3PC in the rats' livers (Table 2), it becomes 2400 μg/L (assuming 1 kg of tissue occupies 1000 ml). Hence, this LOEC is 400 times larger than the largest liver concentration observed, approximately 6 μg/kg of ∑3PC.

The NOAEL for ∑3PC based on the dose given the rats in the in vivo study and the percentage in the CLE mixture is 0.002 mg/kg-day and corresponds to 4.17 mg CLE per ml of corn oil (Table 3).

2.4. Application of uncertainty factors applied to obtain an RfD for tumor promotion

The usual uncertainty factors of 10 for animal-to-human extrapolation and 10 for human variability result in a combined UF of 100. To support this value, it is

Table 4
Margin of exposure for developmental effects among the Inuit based on developmental effects in cultured rat embryos

Chemical	Daily intake (μg/kg-day)	Median maternal plasma or cord blood conc. (μg/L)		Effect level (Calciu et al., 1997, 2002) (μg/L)	Margin of exposure	
		Walker et al. (2003)	Sandanger et al. (2003)		Walker et al. (2003)	Sandanger et al. (2003)
p-26	0.010[a]	0.02	0.05	100[b]	5000	2000
p-50	0.016[a]	0.03	0.09	100	2000	1111

[a] Intakes for p-26 and p-50 were estimated based on median values of 4% p-26 and 6% p-50 (Table 5) and a WT intake of 0.26 μg/kg-day Skopp et al. (2002b), Chan and Yeboah (2000), Chan et al. (1997).

[b] Effect level concentration for TT, p-26 or p-50.

Table 5
Preliminary remediation goals (PRGs) USEPA (2004b) for weathered toxaphene

Medium	Residential soil (mg/kg)	Industrial soil (mg/kg)	Air (μg/m3)	Water (μg/L)
Percentage of ∑3PC in WT	10	10	8.8	5
∑3PC PRG	1.2	12	0.07	0.03
Corresponding WT PRG	12	120	0.8	0.6

necessary to consider possible developmental effects and database insufficiencies, which might add additional uncertainty factors.

2.4.1. Margin of exposure for developmental effects of toxaphene

The rat embryo studies of Calciu et al. (1997, 2002) provide a LOEC value of 100 μg/L. One can compare this value with plasma concentrations in highly exposed humans. Generally, extrapolation from in vitro effects to potential in vivo effects is not typically performed. Nonetheless, a margin-of-exposure (MOE) can be calculated as the ratio between this LOEC and actual plasma levels in these highly exposed humans as an estimate of the likelihood of developmental effects in humans. The larger the value of this MOE, then the less the need for an additional uncertainty factor for possible developmental effects.

Both the Inuit, a circumpolar aboriginal population in Canada and Greenland, and people living in northern Russia, have high intakes of WT because of their dependence on fish and marine mammals as a food source (Arbour et al., 2004; Bjerregaard et al., 2001; Receveur et al., 1998; Sandanger et al., 2003; Van Oostdam et al., 2005; Walker et al., 2003). Mean plasma levels in delivering mothers (Sandanger et al., 2003) and mean umbilical cord blood levels (Walker et al., 2003) of toxaphene congeners can be compared to the LOEC for developmental effects in rat embryos (Calciu et al., 1997, 2002).

Table 4 shows these values and provides a calculation of the ~~margin of exposure for frank effects based on the rat~~ embryo data with p-26 and p-50 as the toxicants (Calciu et al., 1997). The MOEs for both p-26 and p-50 are for both human studies greater than 1000. It is also noteworthy that the rats administered the NOAEL value of CLE failed to accumulate any measurable amount of any toxaphene congeners in their livers (Besselink et al., 2000; MATT, 2000). hence, a much higher external dose than the NOAEL would be needed to produce an internal concentration similar to that of 100 μg/L used by Calciu et al. (1997).

There is no evidence that the Inuit experience greater developmental health effects due to toxaphene exposure than do developed societies (Faustman et al., 2000; Landrigan et al., 2002). Birth defects among the Inuit have been attributed to other causes such as nutrition and alcoholism and increasing "Westernization" of their culture (Arbour et al., 2004; Macaulay et al., 2004). Hence, it is likely that the level of human intake that results in the measured plasma and cord blood levels shown in Table 4 is well below the threshold for developmental effects.

2.4.2. Estimate of a NOAEL based on human intakes of toxaphene congeners

Estimates of daily WT intakes from fish and biota among the Inuit (Chan et al., 1997) can be used to estimate daily intake and compare this to the NOAEL in rats based on GSTp-AHF. The 95th percentile estimated intake for Inuit females is 2.6 μg/kg-day. Using the average percentage value of $\sum$3PC in fish of 22.5% (Table 6), the 95th percentile $\sum$3PC intake would be 0.0006 mg/kg-day, about one-third of the NOAEL value of 0.002 mg/kg-day. Hence, it is very likely that an RfD derived from the rat NOAEL will be protective of developmental effects in humans.

2.4.3. Other potential toxic effects of toxaphene

Other endpoints were considered, although in less detail than those discussed above. These other endpoints were studied using TT, (Andrews et al., 1996; Biessman et al., 1983; Pollock and Hillstrand, 1982; Pollock and Kilgore, 1980; Mohammed et al., 1983). Because of the rapid metabolism and excretion of TT in higher animals and the concept of "auto-testing" as previously discussed, TT studies are appropriate for contributing to the breadth of endpoints considered for $\sum$3PC and contribute to the strength of the database regarding potential effects of $\sum$3PC. However, these other studies are not directly comparable to the NOAEL for $\sum$3PC because the concentration of $\sum$3PC in these studies was not known. However, these studies can be compared to the NOAEL expressed as the dose of CLE, which is 0.6 mg/kg-day (Table 3).

Both Arnold et al. (2001) and Bryce et al. (2001) observed a decrease in serum cholesterol in Cynomolgus monkeys in monkeys given doses of 0.8 mg/kg-day and 1 mg/kg-day respectively. Tryphonas et al. (2000, 2001) observed immunologic effects in Cynomologous monkeys dosed with TT. The NOAEL for these effects is 0.1 mg/ ~~kg-day. Olson et al. (1980) observed neurodevelopmental~~ effects in rats for TT with a LOAEL of 0.5 mg/kg-day. Chu et al. (1988) observed liver effects in rats with a NOAEL of 0.35 mg/kg-day and thyroid effects with a NOAEL of 0.18 mg/kg-day. All of these point-of-departure values are similar to the NOAEL of 0.6 mg/kg-day for the CLE mixture and an uncertainty factor for database insufficiency is not necessary.

2.4.4. Toxaphene congeners and human cancer

With regard to breast cancer specifically, TT, p-26, and p-50 all enhance proliferation of MCF7-E3 human breast cancer estrogen-sensitive cells in vitro (Stelzer and Chan, 1999). In this same cell line, TT, p-26, and p-60 have weak anti-estrogenic properties and can potentially disturb the intracellular signaling mediated by the estrogen receptor (Arcaro et al., 2000; Bonefield et al., 1997) and a link has been suggested between toxaphene and breast cancer. In addition, toxaphene disrupts GJIC and expression of gap junction proteins in normal human breast epithelial cells (Kang et al., 1996). However, the highly expose Inuit have been shown to have very low breast cancer rates, about 1/10 of the average rate in Canada (Gaudette et al., 1996; Miller and Gaudette, 1996).

With regard to cancer, there is also currently no definitive evidence that the circumpolar Inuit experience greater cancer risk due to toxaphene exposure than developed societies. The Inuit present a dissimilar picture when one

Table 6
Percentages of three congeners in total toxaphene concentrations in various biotic samples (based on ng/g wet weight)

Source	%p-26	%p-50	%p-62	%∑3PC	Reference
King Salmon	4.12	5.76	9.41	19.29	Chan and Yeboah (2000)
Dogfish	4.09	5.16	9.14	18.39	Chan and Yeboah (2000)
King Salmon	4.11	6.56	7.67	18.33	Chan and Yeboah (2000)
King Salmon	3.70	6.30	7.26	17.26	Chan and Yeboah (2000)
King Salmon	4.59	6.89	10.00	21.49	Chan and Yeboah (2000)
Whitefish	3.50	6.50	9.75	19.75	Chan and Yeboah (2000)
King Salmon	4.00	5.00	7.67	16.67	Chan and Yeboah (2000)
King Salmon	3.66	5.00	7.93	16.59	Chan and Yeboah (2000)
Trout	3.96	3.96	6.04	13.96	Chan and Yeboah (2000)
King Salmon	3.08	5.94	6.78	15.80	Chan and Yeboah (2000)
King Salmon	5.00	7.42	7.26	19.68	Chan and Yeboah (2000)
Halibut	7.86	9.29	6.19	23.33	Chan and Yeboah (2000)
Ooligan	2.26	2.71	4.71	9.68	Chan and Yeboah (2000)
Chum Salmon	2.84	4.33	6.72	13.88	Chan and Yeboah (2000)
Trout	5.02	6.39	13.24	24.66	Chan and Yeboah (2000)
Trout	4.12	7.41	10.70	22.22	Chan and Yeboah (2000)
Trout	4.42	7.28	13.11	24.81	Chan and Yeboah (2000)
Sockeye	2.29	1.98	3.75	8.02	Chan and Yeboah (2000)
Lake Trout	6.36	5.45	11.82	23.64	Chan and Yeboah (2000)
SRM 1588 cod liver oil	6.38	9.83	4.84	21.06	Chan and Yeboah (2000)
Burbot	2.79	4.12	1.76	8.68	Skopp et al. (2002a,b)
Burbot	6.88	5.74	2.10	14.72	Skopp et al. (2002a,b)
Muskox	0.33	0.45			Skopp et al. (2002a,b)
Beluga	14.01	25.07	0.80	39.88	Skopp et al. (2002a,b)
Narwhal	16.41	20.00	2.24	38.65	Skopp et al. (2002a,b)
Walrus	12.03	6.86	0.33	19.22	Skopp et al. (2002a,b)
Whitefish	13.48	23.60		40.45	Chan et al. (1998)
Lake Trout	10.37	23.70		40.37	Chan et al. (1998)
Narwhal	29.99	25.40		58.05	Chan et al. (1998)
Minimum	0.33	0.45	0.33	8.02	
Maximum	29.99	25.40	13.24	58.05	
Median	4.12	6.39	7.26	19.49	
Average	6.61	8.76	6.85	22.45	

considers the relative frequencies of various types of cancers within the population; however, the etiology remains unclear (Gaudette et al., 1993; Nielsen et al., 1996).

For the reasons of the high MOE for developmental effects, the NOAEL based on human intake estimates, the plethora of TT studies on a variety of endpoints and the lack of concordance of laboratory and human population effects of toxaphene regarding cancer, an additional UF for developmental effects or database insufficiency will not be included and the combined UF is 100. Hence, the RfD for ∑3PC is 2E−05 mg/kg-day.

3. Estimating the risk consuming fish containing weathered toxaphene

From the MATT (2000), the percentages of the three persistent congeners in the corn oil used as a dosing vehicle in the in vitro or in vivo studies (Table 2) are compared with the median values from the fish and shellfish concentrations obtained from sources at northern latitudes (Table 6) or from a Superfund site (Table 7). Note that the percentages of the three congeners are lower in the MATT dosing vehicle than in fish or biota from the environment. The reason for the lower percentage of ∑3PC in CLE may be that TT was weathered in codfish for only two months; over time, toxaphene residues in biota will become enriched in the persistent congeners and the fish and biota data in Tables 6 and 7 were obtained from tissue in which TT had been weathered for years.

As an example of a risk calculation with the ∑3PC RfD derived here, data from fish and shellfish obtained from a Superfund site in the southeastern US were obtained from Maruya (2000). Ninety-five percent upper confidence limits on the arithmetic mean concentrations of WT and ∑3PC concentrations in the fish were calculated with PROUCL software (USEPA, 2004a). Finfish and shellfish concentrations in ng/g wet weight were both included in the calculation. No weighting was used for angler preference of the two types of fish. WT concentrations were generally consistent with a lognormal distribution. Because several nondetect analytical results were present, the bootstrap-*t* method was used for the UCL. The UCL value for WT was 5348 μg/kg. ∑3PC concentrations were consistent with a gamma distribution and the adjusted gamma method was used for the UCL. The UCL value for ∑3PC was 228 μg/kg.

Fish ingestion rates for both children and adults were obtained from Tables 10–61 of the Exposure Factors Handbook (USEPA, 1997a). The highest value of

Table 7
Percentages of the three congeners in total toxaphene concentrations in fish samples from a Superfund site

Source	%p-26	%p-50	%p-62	%∑3PC
Black Drum	2.71			2.71
Blue Crab	6.09	1.50	0.33	7.92
Blue Crab	4.72	2.37	1.09	8.19
Blue Crab	5.39	2.86		8.24
Blue Crab	4.39			4.39
Blue Crab	0.89	0.66		1.56
Blue Crab	2.10	2.15		4.25
Blue Crab	4.45	2.29	0.65	7.39
Blue Crab	4.52	1.20		5.72
Croaker	2.39	0.59		2.98
Croaker	2.32	0.63		2.95
Croaker	2.24	0.41		2.64
Croaker	2.47	0.62		3.10
Mullet	4.19	1.37	0.73	6.29
Mullet	1.94	1.91	0.74	4.59
Mullet	3.62	1.47	0.47	5.55
Mullet	2.59	0.92		3.51
Mullet	3.92	1.23	0.67	5.82
Mullet	0.28	1.43	0.49	2.21
Mullet	3.13	1.50	0.61	5.24
Mullet	4.42	0.69		5.11
Mullet	4.03	1.57		5.60
Red Drum	3.37	1.29	0.64	5.29
Red Drum	2.78	0.88	0.46	4.12
Red Drum	2.85			2.85
Sea Trout	3.92	1.40	0.54	5.86
Sea Trout	0.92	1.05	0.70	2.67
Sea Trout	3.19	0.92	0.53	4.63
Sea Trout	2.54	0.50	0.24	3.28
Sea Trout	2.09	0.57	0.25	2.91
~~Sea Trout~~	~~3.19~~	~~0.70~~	~~0.42~~	~~4.31~~
Sea Trout	3.65	1.04		4.68
Shrimp	4.61	2.84	0.66	8.11
Shrimp	4.42	2.70	0.67	7.79
Shrimp	2.73	1.57	0.55	4.85
Shrimp	4.73	2.74	0.51	7.98
Shrimp	4.06	3.43	1.21	8.69
Shrimp	5.82	1.82		7.63
Spot	3.63	1.24	0.39	5.26
Spot	4.08	1.39	0.29	5.76
Spot	3.72	1.15	0.35	5.22
Spot	3.23	1.02		4.25
Spot	3.51	0.76	0.36	4.63
Spot	2.64	0.52		3.15
Spot	2.79	0.45	0.21	3.46
Spot	3.20	0.65		3.85
Spot	2.05			2.05
Yellowtail	3.20	1.01		4.21
Yellowtail	3.12	0.91	0.35	4.38
Yellowtail	2.98	1.12	0.44	4.53
Flounder	3.54		0.71	4.26
Whiting	3.45			3.45
Minimum	6.09	3.43	1.21	8.69
Maximum	0.28	0.41	0.21	0.00
Median	3.22	1.18	0.52	4.39
Average	3.32	1.33	0.54	4.47

0.369 g/kg-day for consumption of recreationally caught fish is representative of children aged six was used here. Please note that this value will also be protective of adults. In general, site-specific data on fish consumption is preferable to default values such as these. Hence, it may be advisable to obtain site-specific fish consumption data for this Superfund site in the future. In this study, the risk estimates for consumption of fish at this Superfund site are based on these default consumption rates.

$$\mathrm{HQ} = \frac{C_{\mathrm{fish}} \cdot \mathrm{IR}_{\mathrm{fish}}}{\mathrm{RfD}}, \tag{1a}$$

where HQ is the hazard quotient, C_{fish} is the concentration in fish = 228 μg/kg, $\mathrm{IR}_{\mathrm{fish}}$ is the ingestion rate of fish = 0.369 g/kg-day, RfD is the reference dose = 2E−05 mg/kg-day.

Substituting the values and converting units as follows yields a hazard quotient value of 4 for ∑3PC.

$$\mathrm{HQ} = \frac{228\frac{\mu g_{\Sigma 3PC}}{kg_{fish}} \cdot 0.001\frac{mg_{\Sigma 3PC}}{\mu g_{\Sigma 3PC}} \cdot 0.369\frac{g_{fish}}{kg_{BW} \cdot day} \cdot 0.001\frac{kg_{fish}}{g_{fish}} \cdot}{2E-05\frac{mg_{\Sigma 3PC}}{kg_{BW} \cdot day}} = 4 \tag{1b}$$

3.1. Application and development of preliminary remediation goals using the RfD for WT

In applying the RfD for ∑3PC for the development of preliminary remediation goals (PRGs) (USEPA, 2004b) or cleanup levels, back calculation is needed to obtain the PRG concentration of WT that corresponds to ∑3PC based on the percentage of ∑3PC in the ~~WT mixture. There has been considerable and contin~~uing debate over the appropriate analytical methods for WT (de Geus et al., 2000). The key message here is that it will likely be necessary to know the concentration of ∑3PC for risk assessment and this concentration needs to be related to the total WT concentration. This may be possible with a range of analytical methods, but the risk assessor should remain cognizant of this possible pitfall of different results with different analytical methods.

The methodology and exposure assumptions used in the Region 9 Table of PRGs were used to develop PRGs for WT based on ∑3PC. For air, the percentage of ∑3PC in WT was estimated from Bidleman et al. (2004) at 8.8%. For soil, the percentage of ∑3PC in WT was assumed to be 10%; for water, 5%. PRGs for both ∑3PC and WT based on the toxicity of ∑3PC are shown in Table 5. Please note that it is not appropriate to use these WT PRGs as cleanup levels without site-specific determination of the percentage of ∑3PC in WT.

4. Discussion

4.1. Is the CLE representative of WT?

It should be clear from the few (2–5) congeners that comprise the human body burden versus the many congeners present in technical toxaphene (>600) that changes in the composition of the material occurs once released in the environment. A multitude of studies indicate that toxaphene in the environment weathers and the resulting mixture consists of a much smaller number of congeners than in the original TT. As discussed, the persistent congeners that make up the human body burden are p-26, p-50, and p-62. However, a larger number of congeners occur in fish and other biota. The persistence of the various congeners is determined by their thermodynamic stabilities and molecular structural energies (Heimstad et al., 2001). Microbial degradation of toxaphene shows specificity for the removal of chlorines in particular positions on the molecule (Ruppe et al., 2003, 2004). In addition, biotic and abiotic transformation of toxaphene results in different mixtures of congeners (Angerhofer et al., 1999).

Table 6 shows the percentage of the three congeners in biota from a variety of sources (Chan et al., 1998; Chan and Yeboah, 2000; Skopp et al., 2002a). The percentage of p-26 ranges from 0.33 to 30%, p-50 ranges from 0.45 to 25%, and p-62 ranges from 0.33 to 13%. The average percentage of $\sum$3PC in the mixture is 22%. Table 7 shows the percentages of the three congeners from fish samples obtained at a Superfund site collected in 1997 (Maruya, 2000). The percentage of p-26 ranges from 0.28 to 6%, p-50 ranges from 0.41 to 3.4%, and p-62 ranges from 0.21 to 1.21%. The average percentage of $\sum$3PC in the mixture is 4.5%. The samples shown in Table 6 were obtained from fish obtained at northern latitudes that are generally higher in fat than fish obtained from more temperate climates, such as the samples in Table 7. This effect of latitude was also observed by McHugh et al. (2004). Their higher fat content and larger size may be reasons for the higher percentages of $\sum$3PC in the coldwater fish.

Table 8
Calculation of fish ingestion rate for lifetime receptor

Age	Consumption (g/day)	Body weight (kg)	Yearly average fish ingestion rate (g/kg-day)
0	0	9.4	0
1	5.63	11.8	0.477
2	5.63	12.9	0.436
3	5.63	15.1	0.373
4	5.63	17.1	0.329
5	5.63	19.4	0.290
6	7.94	21.7	0.366
7	7.94	25.5	0.311
8	7.94	28.1	0.283
9	7.94	32.7	0.243
10	7.94	35.6	0.223
11	7.27	41.5	0.175
12	7.27	46.9	0.155
13	7.27	55.1	0.132
14	7.27	61.1	0.119
15	7.27	62.8	0.116
16	7.27	65.8	0.110
17	7.27	67.5	0.108
18	7.27	70	0.104
19	7.27	70	0.104
20	7.27	70	0.104
21	10.2	70	0.146
22	10.2	70	0.146
23	10.2	70	0.146
24	10.2	70	0.146
25	10.2	70	0.146
26	10.2	70	0.146
27	10.2	70	0.146
28	10.2	70	0.146
29	10.2	70	0.146
30	10.2	70	0.146
Average for years 0–30			0.194

4.2. Comparison of toxaphene toxicity criteria

One can compare the toxicity criteria for $\sum$3PC with that for TT in terms of fish concentrations. For the TT slope factor, the typical Lifetime Receptor for carcinogenic effects was defined as an individual exposed from age 0 to 30, 6 years as a child and 24 years as an adult. Age-specific body weights and fish consumption rates were obtained from USEPA (1997a). For each year from 1 to 30, the fish consumption rate in g/day was divided by the body weight. These resulting values were averaged over all 30 years to obtain the Lifetime Receptor fish consumption rate (FCR) or 0.194 g/kg-day (Table 8).

The fish concentration representative of a 1E−06 cancer risk using the TT slope factor in a Lifetime Receptor is 0.011 mg/kg. This calculation was performed iteratively by substituting a range of fish concentrations in Eq. (2) shown below until the risk was equal to 1E−06

$$\text{Risk} = \text{CSF} \cdot \frac{C_{\text{fish}} \cdot \text{IR}_{\text{fish}} \cdot 0.001\,\frac{\text{kg}}{\text{g}} \cdot 30\ \text{yr} \cdot 365\,\frac{\text{days}}{\text{yr}}}{25550\,\frac{\text{days}}{\text{lifetime}}} \tag{2}$$

where CSF is the cancer slope factor = 1.1 per mg/kg-day, Risk is the 1E−06, C_{fish} is the concentration in fish (solved iteratively), IR_{fish} is the lifetime fish ingestion rate = 0.194 g/kg-day (Table 8).

The application of the tolerable daily intake (TDI) toxicity criterion developed in (MATT, 2000) or 0.0069 mg/kg-day was performed with Eq. (3). The resulting fish concentration developed corresponding to an HQ of 1 was 35 mg/kg.

$$\text{Acceptable Conc}_{\text{CLE in fish}} = \frac{\text{TDI}_{\text{CLE}}}{\text{IR}_{\text{fish}} \cdot 0.001\ \text{kg/g}}, \tag{3}$$

where TDI_{CLE} is the tolerable daily intake for CLE = 0.0069 mg/kg-day, IR_{fish} is the fish ingestion rate = 0.194 g/kg-day (Lifetime).

The fish concentration of WT representative of $\sum$3PC at 22% of the mixture (Table 6) and at an HQ of 1 for a Lifetime Receptor is 0.45 mg/kg. The fish concentration of WT representative of the $\sum$3PC at 4.5% (Table 7) and at an HQ of 1 for a Lifetime Receptor is 2.2 mg/kg. Eqs. (4a) and (4b) shows this calculation.

$$\text{Acceptable Conc}_{\sum 3\text{PC in fish}} = \frac{\text{RfD}_{\sum 3\text{PC}}}{\text{IR}_{\text{fish}} \cdot 0.001\ \text{kg/g} \cdot \% \sum 3\text{PC}}, \tag{4a}$$

where $\text{RfD}_{\sum 3\text{PC}}$ is the reference dose for $\sum 3\text{PC} = 2\text{E}{-}05$ mg/kg-day, IR_{fish} is the fish ingestion rate = 0.194 g/kg-day (Lifetime), and $\% \sum 3\text{PC}$ is the percentage of $\sum 3\text{PC}$ in the WT mixture.

Substituting values, one obtains

$$\text{Acceptable Conc}_{\text{fish}} = \frac{2\text{E–05 mg/kg-day}}{0.194\ \text{g/kg-day} \cdot 0.001\ \text{kg/g} \cdot 22\%} = 0.45\ \text{mg/kg} \tag{4b}$$

4.3. Toxaphene and human cancers

Toxaphene has been shown to disrupt GJIC in normal human breast epithelial cells and human cancer cells (Kang et al., 1996; Kao et al., 1995). Because of the high fat content of artic marine mammals, these animals represent a reservoir of WT (e.g., Chan and Yeboah, 2000). The Circumpolar Inuit people consume large quantities of marine mammals and are highly exposed to toxaphene relative to the US population with plasma concentrations of WT up to 4 μg/L (Bjerregaard et al., 2001; Sandanger et al., 2003; Walker et al., 2003; Van Oostdam et al., 2005). The Inuit have approximately twentyfold lower breast cancer rates than comparison populations so clearly this concentration is less than a frank effect level.

This additional information indicates that the toxicity assessment presented here is very likely to be protective of tumor promotion in humans and other endpoints as well. Current human exposure to toxaphene is to WT, not TT and the continued use of the more stringent toxicity assessment for technical toxaphene will result in inaccurate risk/hazard estimates and possibly unnecessary and overly costly cleanups.

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Special Contributions

Correspondence about Publication Ethics and *Regulatory Toxicology and Pharmacology*

In this issue, *IJOEH* is publishing correspondence concerning conflicts of interest, lack of transparency, and absence of editorial independence of the journal *Regulatory Toxicology and Pharmacology* (RTP). RTP is the official publication of the industry-funded International Society of Regulatory Toxicology and Pharmacology (ISRTP).

In a letter dated November 19, 2002, the Center for Science in the Public Interest (CSPI) and over 40 scientists (including this *IJOEH* editor) call on Elsevier Press, the publisher and owner of RTP, to hold the journal accountable to norms of publication ethics and to require greater independence of the journal from ISRTP. Elsevier's 11/27/02 reply contests many of the points made in the letter but agrees to implement a policy on conflicts of interest and disclosure for RTP. Elsevier transmits the conflict-of-interest policy in a letter to CSPI dated 1/20/03. The letter dated 1/29/03 is CSPI's reply on behalf of the original signers indicating the deficiencies of the RTP policy.

IJOEH has chosen to publish this exchange in order to alert readers to the ways in which supposedly credible peer-reviewed journals may be co-opted by corporations seeking to give credibility to particular scientific points of view. RTP publishes a large number of studies conducted by industry-funded scientists. These studies later become part of industry efforts to influence federal regulatory agencies or to defend litigation claims concerning toxic exposures. Without safeguards to assure the independence of the editorial process, suspicion—some of it well-deserved—is cast over such studies and journals. —*Editor-in-Chief*

November 19, 2002
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Re: *Regulatory Toxicology and Pharmacology*

Dear Ms. Chrisman and
Mr. Weislogel:

We write to you to express our concerns about apparent conflicts of interest, lack of transparency, and the absence of editorial independence of the journal Regulatory Toxicology and Pharmacology (RTP), which you publish. As you know, that journal is the official publication of the International Society of Regulatory Toxicology and Pharmacology (ISRTP).

Our concerns about Regulatory Toxicology and Pharmacology include:

- The journal's apparent bias in favor of industries that are subject to governmental health and environmental regulations and that provide financial support to RTP's sponsor, ISRTP. ISRTP is supported by, among others, the American Chemistry Council, Bristol-Myers Squibb Company, Dow AgroSciences, Eastman Kodak, Gillette Company, Indspec Chemical Corporation, Merck and Co., Inc., Procter and Gamble, R.J. Reynolds Tobacco Company, The Sapphire Group, Inc., Schering-Plough Research Institute, and SmithKline Beecham Pharmaceuticals—all companies or trade associations that have a direct incentive to minimize the regulatory burden on industry.

- A significant percentage of members of the RTP editorial board has financial ties to companies whose products or by-products are the subject of studies published in RTP. The large number of industry-affiliated scientists and lawyers on the editorial board of RTP is indicative of the pro-industry bias of RTP. Those individuals[1] include:

  - Gio Gori, the editor of RTP (a past vice-president and now council member of ISRTP), has been a paid consultant to Brown and Williamson Tobacco Company and the Tobacco Institute and an outspoken critic of the hazards of environmental tobacco smoke. Documents from tobacco litigation in Minnesota reveal that in 1991 Gori was paid $30,077 by the Tobacco Institute to write the paper "Mainstream and environmental tobacco smoke," which was subsequently published in RTP (1991;14:88-105).

- Louis Lasagna, was a paid consultant to the pharmaceutical companies that made and distributed the diet drug Redux. The consulting arrangement involved testimony at the FDA on behalf of the drug before it was withdrawn from the market because of adverse effects.
- Richard Adamson (National Soft Drink Association)
- Joel Bender (Chief Medical Officer, Owens Corning)
- Johanna Dwyer (consultant for Procter and Gamble, Marlow Foods)
- Gary Flamm (consultant to Philip Morris and Monsanto)
- Jerome Heckman (lawyer for the food and pharmaceutical industries)
- Peter Hutt (lawyer for the food and pharmaceutical industries)
- John Keller (lawyer for the food and pharmaceutical industries)
- Georg Kimmerle (toxicologist, formerly of Bayer AG)
- Steve Lewis (scientist, ExxonMobil Biomedical Sciences, Inc.)
- Roger McClellan (industry consultant and former director of the Chemical Industry Institute of Toxicology)
- Dennis Paustenbach (scientific consultant to industry)
- Robert Scheuplein (scientific consultant to industry)
- Robert Squire (consultant to Procter and Gamble, Calorie Control Council, American Paper Institute)
- Gary Yingling (lawyer for the food, drug, medical devices, and cosmetics industries)

- RTP editorials commonly support industry's anti-regulatory goals. (See e.g., G. Gori, "The costly illusion of regulating unknowable risks," 2001;34:205-212; G. Gori, "The EPA and the courts: inching toward a showdown," 1999;30:167-168; Editors, "Editorial on the interpretive review of potential adverse effects of chlorinated organic chemicals on human health and the environment," 1994;20:xiii.)

- RTP serves as a convenient venue for the publication of industry research and gives the credibility of a peer-reviewed journal to articles that may not have been subjected to full and meaningful independent review. In three recent issues of RTP (2002;35 (1, February), (2, April), and (3, June)), more than 60% of the articles were generated by scientists from industry laboratories. That, and the additional articles authored by industry-funded academics or consultants, are of particular concern given independent studies showing that industry-funded research is lower in quality and more likely to favor the sponsor's product or interests.[2]

- RTP routinely fails to disclose relevant conflicts of interest. In contrast, because of the mounting evidence that financial ties to industry skew research and authors' conclusions in favor of the sponsor's interests, prominent science and biomedical journals have instituted disclosure policies that require publication of relevant conflicts of interest alongside published papers. It is increasingly acknowledged[3] that journalistic ethics requires that:
  - readers be given all relevant information about authors' competing and conflicting interests.
  - editors who make final decisions about manuscripts should have no financial interest in the issues they might judge.
  - editors should not submit their original research to the journal that they edit and, if they do, must recuse themselves from the editorial oversight process.

It appears that policies and practices of RTP reflect none of those principles. Last February a group of scientists wrote a letter (enclosed) to RTP urging the editors to adopt such a policy. RTP never responded.

Given the considerable industry support received by ISRTP, RTP's industry-oriented editorial board, the too-frequent anti-regulatory tenor of RTP's editorials, and the preponderance of publications by industry-funded scientists, we urge Academic Press/Elsevier to increase the credibility of the journal by insisting that RTP (1) sever its ties to the industry-sponsored ISRTP; (2) reconstitute its advisory board to dramatically reduce the influence of industry scientists, industry lawyers, and academic consultants to industry; and (3) adopt an editorial policy of transparency about conflicts of interest. At minimum, the latter would entail disclosing on the masthead (and web site) the relevant industry affiliations of the editorial board members and disclosing relevant financial affiliations of authors whose papers appear in the journal. The affiliations disclosed should include funding sources, consultancies, stock ownership, expert testimony, employment, and others. Consistent with the best interests of an informed public, if the journal fails to take those steps, we urge Academic Press/Elsevier to stop publishing the journal.

Aside from the credibility of RTP and ISRTP, your own reputation as a publisher of credible, peer-reviewed scientific journals is jeopardized by journals that fail to live up to basic journalistic standards as recommended by the Council of Science Editors[4] and the International Committee of Medical Journal Editors.[5]

Thank you for considering our views. We look forward to hearing from you.

Sincerely,

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Please direct correspondence to Virginia A. Sharpe, Ph.D. Center for Science in the Public Interest, 1875 Connecticut Ave. NW, Washington, D.C. 20009.

cc. Sallie W. Carr, Gio Gori

Notes

1. Documentation of some of these ties can be found at <www.IntegrityInScience.org>.
2. See generally, Rochon P. Evaluating the quality of articles published in journal supplements compared with the quality of those published in the parent journal. JAMA.1994;272:108-113; Bero LA, Rennie D. Influences on the quality of published drug studies. Int J Technol Assess Health Care. 1996;12:209-237; Bero LA, Galbraith A, Rennie D . The publication of sponsored symposiums in medical journals. N Engl J Med. 1992; 327:1135-1140; Rochon P, Gurwitz JH, Simms RW, et al. A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. Arch Intern Med. 1994;154:157-163; Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. Ann Intern Med. 1996;124:485-489; Stelfox HT, Chua G, O'Rourke K, Detsky AS. Conflict of interest in the debate over calcium-channel antagonists. N Engl J Med. 1998;338:101-106; DeAngelis C. Conflict of interest and the public trust. JAMA 2000;284:2237-2238.
3. International Committee of M edical Journal Editors. Sponsorship, authorship, and accountability. JAMA. 2001; 286:1232-1234 and <http://www.icmje.org/sponsor.htm>.
4. Editorial policy statements approved by the CSE board of directors. <http://www.councilscienceeditors.org/services_DraftApproved.shtml>.
5. See note 3 above.

Via Facsimile Transmission to 202-265-4954

27 November 2002

Virginia Ashby Sharpe, PhD
Project Director, Integrity in Science
Center for Science in the Public Interest
1875 Connecticut Avenue, NW
Suite 300
Washington, DC 20009-5728

Re: *Regulatory Toxicology and Pharmacology*

Dear Ms. Sharpe:

Thank you very much for coordinating the letter sent to Kirsten Chrisman and Paul Weislogel on 19 November 2002 which lists several concerns that the CSPI and the signatories have with the abovementioned journal. Although some of the issues raised in the letter merit reflection and action, others are unjustified, and factually incorrect. We would like to take this opportunity to reply to these concerns individually.

1. Pro-industry bias

Regulatory Toxicology and Pharmacology (*RTP*) is indeed the official publication of the International Society of Regulatory Toxicology and Pharmacology (ISRTP), and the companies you list in the first bullet point of your letter do support the ISRTP. What your letter does not point out is the fact that academics and ranking government officials also support the ISRTP. Discussions in the journal focus on the *appropriate level* of regulation, not on the minimization or maximization thereof.

Regulatory issues by their very nature affect industry and it is therefore only logical that editorial board members have ties to industry. The ideal editorial board should be balanced, in all senses of the word. We are confident that the editorial board for *RTP* reflects this balance.

Your concern on the editorial slant taken in *RTP* on certain issues is subjective. An editorial by its very nature is an opinion. Should readers disagree with an opinion expressed in an editorial, they are invited to respond with a letter to the editor.

2. Peer Review

All material submitted to the regular issues and the supplements of *Regulatory Toxicology and Pharmacology* is peer-reviewed. Your letter implies that there are various degrees of peer review and insinuates that articles may not have been subjected to "full and meaningful independent review." Although the extent and fairness of peer review is, again, a matter of opinion, we vigorously disagree with your insinuation.

RTP and all other Elsevier journals *are* credible, peer-reviewed scientific journals which not only live up to, but indeed surpass basic journalistic standards and provide valuable information to the research community in both academia and industry.

3. Transparency/Conflict of Interest/Disclosure

The fifth bullet point of your letter raises concerns about transparency and relevant conflicts of interest. We share your concern that journals should have an appropriate disclosure policy to signal possible conflicts of interest. We are therefore pleased to inform you that, by the end of 2002, an appropriate, clear and transparent policy on conflict of interest and disclosure will be put into effect for submissions made to *Regulatory Toxicology and Pharmacology*.

4. Relationship with the ISRTP

RTP's relationship with the ISRTP has been and continues to be a productive one, and we have no intention of encouraging RTP to sever ties with the ISRTP. The conflict of interest/disclosure clause which we will apply will provide the necessary transparency to address the key concerns in your letter.

Thank you in advance for informing the signatories to the letter of our reply. Should you have any further questions, please do not hesitate to contact me, or my colleague Eric Merkel-Sobotta, Elsevier's Director, Corporate Relations, at <e.merkelsobotta@ elsevier.com>.

Sincerely,

Jasna Markovac, PhD
Director, Development
Science & Technology
Elsevier
E-mail: <j.markovac@elsevier.com>

---

20 January 2003

Virginia Ashby Sharpe, PhD
Project Director, Integrity in Science
Center for Science in the Public Interest
1875 Connecticut Avenue, NW
Suite 300
Washington, DC 20009-5728

Re: *Regulatory Toxicology and Pharmacology*

Dear Ms. Sharpe:

As per our correspondence and conversations in November and December 2002, I am pleased to inform you that *Regulatory Toxicology and Pharmacology* (*RTP*) now has a conflict of interest/disclosure policy. The policy has been developed and adopted after extensive discussions with the publisher and the editor of RTP, and we believe it to be appropriate and clear. The policy is as follows:

> Authors are requested to disclose any possible conflicts of interest. Affiliation of authors submitting manuscripts in their role as members of industrial or government organizations may constitute sufficient disclosure. Academic, non-profit, consulting, advocacy, and all other authors are asked to disclose in an appendix section all sources of financial and material support for the studies and manuscripts submitted.

You may also be interested in the fact that, during 2003, Elsevier will decide whether or not we should investigate the need and feasibility of developing a general conflict of interest/disclosure policy for the journals we own.

Should you have any further questions, please do not hesitate to contact me.

Sincerely,

Eric Merkel-Sobotta
Director, Corporate Relations
Elsevier BV

January 29, 2003

Eric Merkel-Sobotta
Director, Corporate Relations
Elsevier Science BV
Sara Burgerhartstraat 25
1055 KV Amsterdam
The Netherlands
fax: 011+31 20 485 28 43

Re: *Regulatory Toxicology and Pharmacology*

Dear Mr. Merkel-Sobotta:

We received your letter dated January 20, 2003 conveying the conflict-of-interest/disclosure policy for *Regulatory Toxicology and Pharmacology*. As Elsevier considers the question of a general conflict-of-interest/disclosure policy for the journals it owns, we strongly discourage using the *RTP* policy as a model.

The policy has numerous deficiencies including:

- Disclosure by authors is voluntary, not mandatory.
- There is no declaration that author disclosures will, in fact, be published with the article. There is no explanation of what, if any, procedures the editors will use to determine which disclosures, if any, will/will not be published.

- Disclosure is limited to employment-affiliation and financial or material support only *for the particular paper submitted.* This means that a scientist who routinely consults for industry or provides expert testimony for industry but received no industry support for the particular paper, would not be required to disclose those other ties. It also excludes disclosure of support from industry to the institutions where authors work (e.g., financial and material support not exclusively used for the specific project being described in the manuscript).
- An author's disclosure of his or her government affiliation is deemed sufficient, however, this ignores the fact that some government science is co-sponsored by industry.
- The policy is silent on the matter of authors identifying and affirming their specific role(s) in the production of the paper.
- The policy is silent on the practice of editors having a financial interest in manuscripts they are asked to judge.
- The policy is silent on the practice of editors submitting original papers to journals that they edit.
- The policy is silent regarding the publication of papers over which the sponsor has control of data or the decision to publish results.
- The policy is silent on the matter of disclosure by *RTP* editorial board members of their industry affiliations.

There are a number of exemplary statements on conflict of interest and publication ethics that Elsevier could have acknowledged or endorsed in this policy. Instead, Elsevier has offered a mediocre and perfunctory response to the very real problem of industry influence on scientific research—and *RTP*'s role in contributing to that problem. The weakness of the policy only reinforces *RTP*'s status as an outlier among peer review journals.

If Elsevier does decide to develop a general conflict-of-interest policy for its 1500 journals, this would be—by every available measure—a very sorry model indeed.

Sincerely,

VIRGINIA A. SHARPE, PH.D.
Project Director, Integrity in Science

cc. Gio Gori

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Congressional
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Memorandum May 2, 2008

TO: House Oversight and Government Reform Committee
Attention: Ali Ahmad

FROM: Deborah D. Stine
Specialist in Science and Technology Policy
Resources, Science, and Industry Division

SUBJECT: Methodological Analysis of Union of Concerned Scientists Report on Political Interference at EPA

This memorandum is in response to your inquiry requesting a methodological analysis of the Union of Concerned Scientists' (UCS) report, *Interference at the EPA: Science and Politics at the U.S. Environmental Protection Agency.*[1] You requested a critique of Appendices A (survey text and responses), B (selected survey results), and C (CSSM methodology report) of this report, focusing on the fairness of the questions and the statistical soundness. Provided below is a brief summary of the report's methodology, followed by a critique of the analysis in the report.[2]

UCS Report Methodology

UCS worked with the Survey Research Services, Center for Survey Statistics and Methodology (CSSM), Iowa State University on this report. The questions were developed by UCS as was the report. CSSM consulted on project development, implemented the data collection process, and assisted in data analysis. CSSM's report (Appendix C) describes some of the challenges of the analysis.

The list of individuals sampled in the survey were compiled by UCS using online public records. CSSM then contacted these individuals in several waves, including reminder emails, from June 25, 2007 until August 30, 2007. Those who chose to respond did so via the web. Data collection ended on September 30, 2007. A total of 1,583 responses were received from an adjusted eligible sample of 5,814, providing a 27.3% response rate according to CSSM or 29.3% according to UCS (see further discussion of this below). The resulting report provides the frequency of responses — both the number and percentage of respondents for a particular answer — to 44 questions.

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[1] Union of Concerned Scientists, *Interference at the EPA: Science and Politics at the U.S. Environmental Protection Agency*, April 2008 at [http://www.ucsusa.org/assets/documents/scientific_integrity/Interference-at-the-EPA.pdf].

[2] Royce Crocker, Specialist in American National Government, Government and Finance Division, also contributed to this memorandum in the discussion of political interference and statistical soundness.

Fairness of Questions

Fundamentally, one's perception of "fairness" will differ according to who is reviewing the question. As a result, there is no objective criteria for whether or not a question is fair. Measuring bias is possible. To undertake this analysis, however, would require that the same question be asked in different ways to determine if the same results were achieved regardless of how the question was asked. It is not possible to undertake such an analysis in the time available. As a result, the analysis in this memorandum attempts to provide no more than a critique of the UCS questions. Several issues regarding the fairness of the question and the reporting of the related results include the vagueness in term definitions, the need for a control group, and the need for longitudinal analysis. These are discussed in more depth below.

Term Definition. One general issue regarding the questions is the lack of definitions for some terms. For example, the definition of "scientific work" is somewhat vague, so respondents may have different interpretations. Terms used in the survey questions ranged from "appropriate time and resources" to "political interference."[3]

For example, political interference or the charge of political interference at EPA has been an issue for some time. But, exactly what constitutes such interference, as opposed to editorial differences and policy or substantive disagreements, is not spelled out for the respondents. ~~One person's political interference might be another's heavy handed editing.~~ While under many circumstances, it is appropriate to let the respondents build their own views of what is being asked, it is also important to construct questionnaires that provide the same stimulus to the subjects. If each respondent views political interference in a different way, then interpreting the results becomes subject to challenge. While the study did explore various aspects of "political interference," it is not clear whether or not this phrase, in and of itself, created a context that may have influenced how respondents interpreted questions. Again, without further research, one can only speculate about such an effect. However, as all of the questions dealing with political interference came at the end of the questionnaire, it is less likely that the responses to earlier questions were affected.

Control Group. Many scientific studies rely on the use of a "control group." The purpose of the control group is to isolate a particular variable – in this case, EPA. The goal would be to have two similar groups, keeping all variables constant such as the type of respondent (e.g., scientists) and the questions asked, except for the variable of interest (e.g, organization). This is somewhat challenging in surveys, but having a comparison group where similar respondents in another organization were asked the same questions about their organization and its management would have been useful to understand the degree to which the EPA scientists' views differ from that of another organization's scientists. If such a control group model were used, then it would be possible to determine if there were statistically significant differences between the two sets of respondents.

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[3] Examples of other terms used in the survey whose meaning may vary relative to the respondent are integrity and professionalism, effectively and effectiveness, sufficient, impaired, consistently stands behind, best judgment, satisfaction, complete and accurate, speak freely, inappropriately involved, inappropriately induced, incomplete, inaccurate, and misleading, inappropriately exclude or alter, unusual administrative requirements, and misrepresent.

For example, question 34 of the survey asks "How often have you personally experienced the following situation?...Changes or edits during review that change the meaning of scientific findings?" The results of the responses to this question would have greater meaning if it could be compared against a norm of some kind. Supervisors commonly edit work. Scientists commonly disagree with one another. A senior scientist may overrule, due to their experience, a junior scientist. A junior scientist may believe they are more up-to-date than a senior scientist, and as a result, believe that their interpretation of a scientific finding differs from that of the senior scientist. At what point is it appropriate to call such changes and edits "political interference" as is done in the UCS report? Without a norm by which to judge such responses, it is difficult to interpret the meaning of the result.

Longitudinal Analysis. Another related issue is the degree to which the responses to these questions has changed over time. Would the responses have been the same or different during previous Presidential administrations? Even within an administration, the handling of issues may differ relative to who is appointed as EPA Administrator and who holds other major political positions at EPA. Further, the education and training of those individuals may differ. For example, a manager with a scientific and technical background may have a different view of a situation than one trained as a lawyer. There is some attempt to gain an understanding of the need for longitudinal comparison data in question 40 which asks

> If you compare the past 5 years to the 5-year period prior to it (from 5 to 10 years ago), ~~would you say [political interference] activities or situations like those listed above are~~ occurring:

	Survey Responses
More often than before	34.4%
About the same as before	22.4%
Less often than before	4.4%
Don't know	38.8%.[4]

This question has several challenges to it. The first is that the question does not provide a mechanism for determining whether or not the respondent has been working for EPA for 10 years before determining if they are an appropriate respondent. This may be an indicator for why the "don't know" response is highest for this question relative to the others in the survey. Second, the 5-10 year time frame is a range, so that some respondents will be reporting their perceptions within the same administration, while others will be reporting their perceptions of the previous administration.

To address the issue of time frame relative to experience on question 40, the report uses the available demographic data to break out the responses for this question relative to the years the respondent has worked for EPA.

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[4] *Interference at the EPA*, p. 74.

	Survey Responses Years Working at EPA 11-15	 More than 15
More often than before	40.3%	42.9%
About the same as before	20.9%	29.1%
Less often than before	6.7%	4.1%
Don't know	32.1%.	23.8%.[5]

One challenge with this data is that it is possible that some of the individuals with that degree of experience are now the managers.

Question 13 is another question that takes into account the time frame:

Compared to five years ago, the effectiveness of my division or office has

	Survey Responses
Increased	20.6%
Stayed the Same	24.9%
Decreased	44.6%
No Opinion	9.9%

This question could be a factor resulting in a lower percentage in the "no opinion" category — providing a defined 5-year period within the same Administration.

Hearsay. A number of questions rely on what a respondent "knew of," commonly termed "hearsay." In other words, what people have heard rather than what they have themselves experienced, which as a result, may not be reliable as they are subject to flaws in memory or perception. For example, question 25 in the section under political interference, asks "How many cases do you know of where the following situations have occurred? . . .Cases where EPA political appointees have inappropriately involved themselves in scientific decisions."

Statistical Soundness[6]

Several issues regarding the statistical soundness of the UCS analysis include who is being sampled, the response rate, questionnaire order, and data presentation. These issues are described in more depth below.

"Sample". The results of the study are not based on a probability "sample," but rather a census of eligible "scientists" at EPA with a limited response rate.[7] The study is based on responses to the questionnaire from scientists at the EPA. Most scientists who could be identified by UCS were included in the survey, and just under 30 percent responded. Consequently, there are no issues related to sampling errors as there was no probability sample.

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[5] *Interference at the EPA*, p. 84.

[6] This section was written by Royce Crocker, Specialist in American National Government, Government and Finance Division.

[7] A census is a total count of some population–people, cars, tulips or EPA scientists. A sample of that population is a subset of the population, usually selected using some prescribed procedure. In the case of a probability sample, members of the population are, at a minimum, selected to be included in the sample with some known probability (e.g., one in ten, one in five). It would appear from the report that the UCS intended to interview as many EPA active scientists as they could. If (continued...)

Chapter 3 of the report offers a relatively clear description of the limitations of the attempts to define the population under study, as noted by the authors in the following excerpts.

> To allow as many EPA scientists as possible to participate, we erred on the side of including employees who worked at scientific branches and divisions even if their job duties were unclear. The mailing list was therefore broad but of uneven quality.[8]
>
> ...in divisions that posted names but not job titles, the sample likely included some nonscientists. Conversely, the survey may have improperly excluded some legitimate scientists working in divisions where Internet search was the primary means of obtaining information. This approach produced a notable bias toward agency veterans, as their names were more likely to appear on a website, at the expense of younger scientists, and new hires.[9]
>
> We used a broad definition of "scientist"when compiling the mailing list.[10]
>
> The survey was designed to measure raw numbers of scientists who experienced political interference in their scientific work. Because of unknown selection effects in creating the sample, the self-selection of respondents, it is difficult to extrapolate these raw numbers to a percentage of the EPA's total scientific workforce.[11]

Each one of these limitations has implications for any analysis of the data. The list of scientists eligible to be included in the study, as provided to the CSSM, was not clearly defined with respect to the studied population. It included nonscientists as well as scientists, and, as noted above, was likely to be biased toward more senior scientists (i.e., arguably those who were most likely to question anyone's authority or ability to review their work). The fact that the results of the survey were not designed to provide extrapolations to the total population, while noted in Chapter 3, is not made as clear in the rest of the report.

Response Rates. According to the UCS report, the response rate was 29.3 percent.[12] However, the CSSM's report indicates that the response rate was 27.3 percent. The discrepancy may be attributed to the fact that the UCS researchers incorrectly excluded 395

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[7] (...continued)
they were successful, the report would have been based on all EPA active scientists — a census of EPA scientists. The fact that the UCS was unable to accomplish their goal does not create a sample, but rather a census with significant limitations.

[8] *Interference at the EPA*, p. 20.

[9] Ibid., p. 20.

[10] Ibid., p. 21.

[11] Ibid. p. 21.

[12] Ibid., p. 21.

individuals from the "sample" due to the fact the UCS could not discover e-mail addresses associated with these individuals. CSSM correctly included these individuals in calculating the study's response rate.[13]

While almost 6,000 employees were given the opportunity to participate in the study, a little less than 30 percent completed a questionnaire. Thus, while it may be true that 889 persons at EPA experienced at least one incident of, what the respondents interpreted or accepted UCS's label as, "political interference" during the past five years,[14] this constituted 56.0 percent (889/1586) of those completing the questionnaire, and 15.3 percent (889/5814) of those included in the population under study. This comparative calculation could have been done on all results from the study, producing equally valid figures, depending on what one wanted to emphasize.

Non-response to a survey generally may make it difficult, if not impossible, to project to a larger portion of a population. That is not at issue here, however. This is not a sample survey, but rather a census. For the results of this survey, non-response not only means that the views on the issues dealt with in the questionnaire of over 70 percent of the eligible "sample"/population are not known, but, in this case, it potentially makes the presentation of the data lead to different conclusions. The reader does not know whether the numbers should be viewed as a proportion only of those responding or, because all had an opportunity to participate, as a proportion of the whole population (i.e., all scientists in the agency) under study. As shown above, the two different calculations might lead the reader to different conclusions.

Questionnaire Order. It is difficult to evaluate the questionnaire as it is clear from the CSSM's presentation that the web-based questionnaire included table format questions ~~and was designed using the Tailored Design Method (TDM).[15] As there is nothing like such~~ a questionnaire in the report, one must assume that the original questionnaire is not included. At best, there is a list of questions with their marginal results included in Appendix A.[16] Assuming that the order of the questions shown in Appendix A corresponds to the order of the questions in the original questionnaire, there does not appear to be any obvious order effects. However, to verify this one would need to alter the order of the questions in another similar survey to actually gauge if there are any differences. Even then one could only speculate as to which order resulted in which effect and which order was less 'biased.' That level of research exceeds our resources given the deadline presented to CRS.

Presentation of the Data. The Union of Concerned Scientists are advocates of a point of view; therefore, it is not unrealistic to believe that any study sponsored by them will likely emphasize that point of view. This is not meant to be a criticism of the approach taken, simply a recognition of the organization's advocacy role.

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[13] For a full description of the criteria used by most survey researchers in calculating response rate, non-response rate, and related terms, see: AAPOR, *Standard Definitions*, The American Association for Public Opinion Research (AAPOR), *Standard Definitions, Final Dispositions of Case Codes and Outcome Rates for Surveys*, 4th edition, (Lenaxa, Kansas, AAPOR, 2006), esp. pp. 32-34, at [http://www.aapor.org/uploads/standarddefs_4.pdf].

[14] *Interference at the EPA*, p. 2.

[15] Ibid., p. 89.

[16] Ibid., p. 69-74.

What the presentation of the data does not point out are the limitations of the data. The UCS's report does provide sufficient information for any analyst to examine, and it highlights some of those limitations even if the UCS did not feel that a thorough examination was necessary. For example, while the study presents the actual number of respondents who chose a particular answer, percentages are also calculated. While this is often useful in such a study, it becomes somewhat confusing when it is not clear what the percentages actually mean. This appears to be the case in the calculation of percentages for each of the divisions within EPA.[17] It is not clear whether the denominator of the percentages is all of the respondents in the study or all of the respondents in each of the divisions.

In addition, an examination of the results for each question shown in Appendix A includes results for all types of responses. In the body of the report, there is little or no mention of the "No Opinion" responses. However, in 12 out of 14 questions reporting the results for this category, the percentage choosing the "No Opinion" option exceeded 15 percent. In 7 of the 14 questions, this response exceeded 20 percent. When a fifth to a third of a survey's respondents provide "No Opinion" responses to questions, some of which were important for the conclusions reached in the report, some analysis of these responses might seem appropriate, as well as a discussion of how these responses might affect the conclusions reached, if at all.

Summary

This review of the UCS report identified the following analytical issues:

- Some terms and phrases used in questionnaire are vague, so respondents may have made different interpretations of their meaning, which may have influenced their responses.
- A control group was not included in the analysis, so it is difficult to determine whether survey respondents views of EPA managers differ from that of other science and engineering workforces and their managers.
- A longitudinal analysis was not conducted, so it is difficult to determine whether responses from EPA's current workforce would have differed from those who worked in past administrations.
- Some questions relied on what the respondent "knew of" (hearsay) rather than what the respondent personally experienced.
- The respondents likely included those beyond the intended sample such as non-scientists and was biased toward senior scientists.
- The sample is not designed so that results can be extrapolated to a total population (a condition which is not made clear throughout report).
- The response rate stated by UCS (29.3%) differs from that of CSSM (27.3%). While CSSM does provide the response rate, UCS instead provides what is called a cooperation rate.
- The percentages in the report were calculated using the total response population as the base (usually 1,586). It would have been equally valid to calculate the responses over the entire "sample" (both respondents and non-respondents) indicating what proportion of all scientists at EPA (5814, as determined by UCS) held the views. The two percentages might lead one to draw different conclusions about the magnitude of EPA scientists who

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[17] Ibid., pp. 26-27, figures 7-8.

held particular views. For example, using the total response population as the base, 56.0% of respondents indicate that they experienced at least one incidence of political interference, but it would be 15.3% if the entire sample were used as a base.
- The original questionnaire and data limitations are not included in analysis.
- The conclusions drawn from the analysis may be inappropriate in instances in which the "No opinion" responses to a question exceed 20%.

Although this memorandum has outlined analytical issues with regard to the UCS survey and the resulting analysis, UCS did provide a generally transparent overview of their analysis, and brought in a qualified organization, CSSM, to help. In addition, it is difficult to tell whether or not any of the critiques identified above would change the public's perception of the survey results regarding the issue. Further, it is important to keep in mind that for many in the science and engineering community, even one case of political interference would be considered to be improper. Independence is a critical part of this community's value system, regardless of whether they are working for government, universities, or industry.

On the other hand, UCS does extrapolate this survey perhaps farther than it should in its report. For example, UCS states

> The results of these investigations show an agency under siege from political pressures. On numerous issues—ranging from mercury pollution to groundwater contamination to climate change—political appointees of the George W. Bush administration have edited scientific documents, manipulated scientific assessments, and generally sought to undermine the science behind dozens of EPA regulations.[18]

However, depending on the population base used, the percentage who personally experienced at lease one incidence of political interference is either 56.0% or 15.3%, which may influence one's perception of whether or not EPA is "under siege." In addition, the survey respondents were not asked questions about specific environmental issues such as the those in the quote — mercury pollution, groundwater contamination, and climate change — so it is unknown as to which environmental issues survey respondents were referring to when they indicated that political interference had taken place.

I hope this information is responsive to your request. If you have any additional questions regarding the material in this memorandum, please do not hesitate to contact Deborah Stine at 7-8431 or dstine@crs.loc.gov or Royce Crocker at 7-7871 or rcrocker@crs.loc.gov.

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[18] Ibid., p. 2.

Response to Congressional Research Service "Methodological Analysis of Union of Concerned Scientists Report on Political Interference at EPA"

Timothy Donaghy[1] and Francesca Grifo
Scientific Integrity Program
Union of Concerned Scientists

In May 2008, the Congressional Research Service (CRS)[2] reviewed the methodology of a report by the Union of Concerned Scientists (UCS) titled *Interference at the EPA: Science and Politics at the Environmental Protection Agency.*[3] UCS staff obtained a copy of the CRS analysis during the May 20, 2008 hearing of the House Oversight and Government Reform Committee regarding the EPA's new ozone standard.

We found the CRS report to be even-handed but lacking in concrete criticisms of our report and conclusions, instead identifying "challenges" and "issues." In particular, the CRS report did not expose any flaws with our methodology that would invalidate our conclusions. However, we do want to correct certain inaccuracies in the report and highlight areas where we disagree with CRS conclusions. We would like to thank Chairman Waxman, Ranking Member Davis and the committee members for the opportunity to submit this statement.

Overview

The primary conclusion of the UCS report is this: large numbers of scientists working at the EPA report personally experiencing inappropriate interference in their scientific work. This conclusion is firmly supported by our methodology and analyses. The CRS report does not ~~identify any issues that would invalidate that conclusion. Rather, the CRS report identifies~~ several issues where additional information would have enabled further analysis or where differences of opinion might exist in interpreting the data.

Our survey methodology does *not* support extrapolating our findings to the EPA's entire scientific workforce. We intentionally made this point explicit in the report's methodology section, in presenting the survey findings in the report and in all communications related to the report.

The CRS report acknowledges that this emphasis on raw numbers is a valid means of measuring interference, stating: "It is important to keep in mind that for many in the science and engineering community, even one case of political interference would be considered to be improper. Independence is a critical part of this community's value system, regardless of whether they are working for government, universities or industry."[4]

In presenting our research results our goal was to be fully transparent, and to present evidence of a serious problem at EPA without extending the survey data beyond what is defensible. In addition to working with Center for Survey Statistics and Methodology at Iowa State University to design and implement the survey, the report was also reviewed by numerous independent experts, several of whom had experience working for the EPA or other federal science agencies. The CRS report acknowledged the transparency of our methodology, stating: "Although this memorandum has outlined several issues with regard to the UCS survey and the resulting analysis, UCS did provide a generally transparent overview of their analysis, and brought in a qualified organization, CSSM, to help."[5]

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[1] Email: tdonaghy@ucsusa.org

[2] Stine, D. and R. Crocker. 2008. "Methodological Analysis of Union of Concerned Scientists Report on Political Interference at EPA," May 2. Washington, DC: Congressional Research Service.

[3] Union of Concerned Scientists. 2008. Interference at the EPA: Science and Politics at the U.S. Environmental Protection Agency. April. Washington, DC. Available online at http://www.ucsusa.org/EPAscience/.

[4] CRS, p. 8.

Finally, many of our survey design choices were driven by the fact that we are an organization working outside the federal government attempting to shine a light into a mostly non-transparent agency. Our "outsider" status limited our ability to obtain a complete list of scientists and to achieve full participation in the survey. To fully address many of the issues raised by CRS would require the full cooperation of the EPA and the Office of Personnel Management (i.e. access to full staff lists and encouragement of employees to complete the survey). In the interest of strengthening the EPA to fulfill its critical mission, we are more than willing to cooperate with EPA leadership in any future assessments of political interference at the agency.

In the following sections, we response to each of the issues raised in the CRS report.

Fairness of Questions

The CRS report acknowledges that there are "no objective criteria" for measuring the fairness of a survey question and did not attempt to test our questions for possible bias. Instead, the CRS authors speculate that the vagueness of some terms in the survey may have influenced the responses.[6] Because the CRS report does not make any concrete claims about these issues, we discuss the reasoning behind the choices we made when designing the survey. The CRS report also identifies two further types of analysis that could provide additional information about science at the EPA, but were beyond the scope of our study.

Term Definition

> "Some terms and phrases used in questionnaire are vague, so respondents may have made different interpretations of their meaning, which may have influenced their responses."[7]

The CRS authors correctly note that the term "political interference" is open to a variety of interpretations, as are other terms used in the questionnaire. However the term "political interference" itself appears only twice in the survey instrument, first as a section header before Question 25 and secondly in the text before Question 39. Questions 29 through 38 ask more specific questions about various forms of interference.

These 10 questions are also open to interpretation. We strove to make these questions as focused as possible and yet still be applicable across the entire agency. Questions that focus narrowly on a specific EPA program or a specific issue would avoid some of this vagueness, but such specificity was beyond the scope of this study. Because of this, we relied on the expertise of the respondents to identify what they regarded as inappropriate interference in their work.

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[5] CRS, p. 8.
[6] CRS, p. 5.
[7] CRS, p. 7.

The CRS also speculated that use of the term "created a context that may have influenced how respondents interpreted questions." We designed the survey to ask about specific types of interference (Questions 25-38) before the general question about the number of incidents of interference of all types (Question 39). In our view, the enumeration of these specific types of interference helped to define the context for the survey respondents more specifically than the general term "political interference." Because the survey was administered electronically, respondents could not see Question 39 before any of the other questions.

Control Group

> "A control group was not included in the analysis, so it is difficult to determine whether survey respondents views of EPA managers differ from that of other science and engineering workforces and their managers."[8]

This is a valid criticism, and in past surveys we have employed a control group as a means of comparison with the federal scientific workforce. For this survey, we struggled to identify an external group with comparable scientific and regulatory duties to compare against such a large and complex agency as the U.S. EPA. The lack of an external control group is another reason that we focus on the raw numbers of respondents experiencing political interference and do not attempt to extrapolate our results to the entire EPA scientific workforce.

To address this problem, we did compare rates of interference across the internal offices and divisions of the EPA. This analysis showed that the basic science divisions experienced broadly lower rates of interference than did divisions with regulatory responsibilities. This is an imperfect control group, but it does give some indication that the rates of interference seen at ~~some parts of the~~ EPA ~~are not a necessary consequence of scientific work or ordinary office~~ disputes.

Longitudinal Analysis

> "A longitudinal analysis was not conducted, so it is difficult to determine whether responses from EPA's current workforce would have differed from those who worked in past administrations."[9]

A full longitudinal analysis is beyond the scope of this survey. The ideal would be to have information on political interference taken from periodic surveys with consistent question wording. Such information, while highly interesting, can't be obtained from a single survey and, as far as we know, does not currently exist. In an attempt to understand trends over time, we included question 40, which asks respondents to compare rates of interference over the past five years with the five-year period preceding it.

The CRS report criticizes our use of data from question 40, but the authors seem to not have read our discussion of those results in the main text. The CRS report states that question 40 "does not provide a mechanism for determining whether or not the respondent has been working at EPA for 10 years before determining if they are an appropriate respondent." The report *does* mention our use of demographic data to fully address this concern, but it leaves the impression that we buried this information in the appendix. On the contrary, when we discuss this statistic in the main text of the report we only cite results from this question for respondents who had been with the EPA for greater than 10 years.[10]

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[8] CRS, p. 7.
[9] CRS, p. 7.

The CRS report also critiques the time frame used in question 40. It is true that the time frame under consideration—from five years ago to ten years ago—overlaps two administrations. However, the obvious alternate wording of the question (asking respondents to explicitly compare the current administration against the previous administration) would risk introducing a partisan bias to the question and would complicate our use of demographic data in understanding the results.

Hearsay

> "Some questions relied on what the respondent "knew of" (hearsay) rather than what the respondent personally experienced."[11]

This is a valid concern, but not one that detracts from main conclusions of the report. Four survey questions (25-28) deal with how many incidents of interference respondents "knew of", whereas ten survey questions (29-38) asked about personal experience with specific types of political interference. In our discussion of these results we are careful to use the results of question 25-28 only to shine light on the *culprits* of political interference (i.e. political appointees, other federal agencies, etc.). In assessing the *magnitude* of various types of interference, we rely on questions 29-38.

Statistical Soundness

"Sample"

> "The respondents likely included those beyond the intended sample such as non-scientists and was biased toward senior scientists."[12]

We strongly disagree that the survey respondents included "those beyond the intended sample such as non-scientists." In writing about this issue, the CRS authors conflate our acknowledgment of the limitations of the *initial sample* with limitations of final set of survey respondents. Notably, CRS does not mention our use of responses to question 2 to screen out non-scientists who were improperly included in the initial mailing list. In fact, we excluded all survey respondents who reported that zero percent of their job duties included scientific work.

We deliberately sought to include EPA employees who do scientific work even though they may not have academic training in a scientific field. Such employees are a significant part of EPA's scientific enterprise. Sixty-six respondents reported their major field of training was "Non-Science" but that some percentage of their job duties involved scientific work.[13]

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[10] UCS, p. 2 and p. 24-25.
[11] CRS, p. 7.
[12] CRS, p. 7.
[13] UCS, p. 69.

As we stated in the report, it is likely that the survey respondents are biased towards more senior scientists. This is due both to limitations of the initial sample and self-selection of those responding to the survey. A more complete sample would certainly be desirable, but we disagree that a bias towards senior scientists weakens the conclusions of the report.

Response Rates

> "The response rate stated by UCS (29.3 %) differs from that of CSSM (27.3 %). While CSSM does provide the response rate, UCS instead provides what is called a cooperation rate."[14]

As noted in the CRS report, there is a discrepancy between our quoted response rate (29.3%) and that reported by CSSM and reproduced in Appendix D (27.3 %). This discrepancy arises because we excluded from the eligible sample 395 individuals whose email addresses were returned as undeliverable and whose names did not appear in the EPA's online employee locator. We made this decision because a listing in the online employee locator was a requirement for inclusion when we created the initial sample; with this in mind, we strove for consistency in reporting the final data as well.

In deciding to report a rate of 29.3% we discussed our reasoning with CSSM experts who informed us that such a decision was valid. In the interest of full disclosure we included CSSM's rate as part of Appendix D and added a note explaining the discrepancy. In retrospect, we should have provided more explanation for our decision in the main body of the report and we regret any confusion that it might have caused.

~~Questionnaire Order~~

> "The original questionnaire and data limitations are not included in analysis."[15]

The order of questions and response options in the actual web survey questionnaire is identical to that presented in Appendix A (except for the re-coded response options described there). The original questionnaire text was not included in the report for space reasons but we are happy to make the text available upon request. CRS's discussion of questionnaire order states that there "does not appear to be any obvious order effects."[16]

Presentation of the Data

The CRS report highlights some questions regarding our presentation of the data, but we argue that these concerns are based in part on misreadings of our report.

> "UCS does extrapolate this survey perhaps farther than it should in its report. [...] In addition, the survey respondents were not asked questions about specific environmental issues such as those in the quote ... so it is unknown as to which environmental issues

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[14] CRS, p. 7.
[15] CRS, p. 8.
[16] CRS, p. 6.

> survey respondents were referring to when they indicated that political interference had taken place."[17]

As evidence for this over-reaching, CRS cites a passage referring to specific instances of political interference at the EPA—namely mercury pollution, groundwater contamination and climate change.[18] However, CRS's claim is based on a misunderstanding of the cited passage. In addition to the survey results, the UCS report also includes case studies that draw on interviews with EPA scientists, government documents and media reports to document specific examples political interference. The three examples mentioned in the passage are included not because we deduced these issues from the survey results, but because we examine each of them in detail in other sections of the report.

The confusion here may be a result of the narrow charge placed on the CRS researchers,[19] who may have focused on the sections of the UCS report discussing survey methodology and may not have read the sections containing the case studies.[20]

> "The percentages in the report were calculated using the total response population as the base (usually 1,586). It would have been equally valid to calculate the responses over the entire "sample" (both respondents and non-respondents) indicating what proportion of all scientists at EPA (5814, as determined by UCS) held the views. The two percentages might lead one to draw different conclusions about the magnitude of EPA scientists who held particular views. For example, using the total response population as the base, 56.0% of respondents indicate that they experienced at least one incidence of political interference, but it would be 15.3% if the entire sample were used as a base."[21]

One minor technical clarification: the percentages in the report were calculated using the number of respondents answering the given question as a base. This number is not "usually" 1,586 as CRS states; for a given question it is always smaller than 1,586 because no question was answered by 100% of the respondents. For the question considered in the quote above (question 39), the total number of respondents is 1,470 yielding the 60 % (889/1470) that we quote in the report, rather than the 56% that CRS calculates. The base for these percentages can be found in Appendix B for selected questions (see the row labeled "Total"), and for the rest can be calculated by summing the response options listed in Appendix A.

The larger question of "what level of interference constitutes a problem for the agency" is certainly subject to differing opinions. Indeed, our main conclusion is that, regardless of what percentage of EPA's workforce it reflects, the number of scientists who reported political interference is unacceptably large. In response to questions from members of Congress about our report, EPA's Science Adviser George Gray stated that such a large number of scientists reporting interference was "unacceptable" to him as well.[22]

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[17] CRS, p. 8.

[18] UCS, p. 2.

[19] CRS, p. 1, "You requested a critique of Appendices A (survey text and responses), B (selected survey results), and C (CSSM methodology report) of this report, focusing on the fairness of the questions and the statistical soundness."

[20] UCS, Chapters 4-7.

[21] CRS, p. 7.

[22] Grey, G. 2008. Testimony before the Senate Environment and Public Works Committee, May 7.

However, as CRS states, our method for calculating percentages is "equally valid" and we feel we have provided enough information for readers to make up their own minds on this point.

> "The conclusions drawn from the analysis may be inappropriate in instances in which the 'No opinion' responses to a question exceed 20%."[23]

Again, our conclusions are based on the raw numbers of respondents, not the percentage that number represents, so it is unclear what a threshold of 20% implies for our conclusions. Many of the questions with a large percentage of "No Opinion" responses deal with specific issues with which a given respondent may not have had experience.

An example of a question with more than 20% of respondents choosing "No Opinion" involves closures to parts of EPA's library system (question 16). In this case, we highlighted the fact that over 500 scientists felt the library closures had impaired their ability to do their job—a highly relevant piece of information when evaluating the usefulness of the library system. Yet the large number of respondents with "No Opinion" may reflect the fact that only certain regions and offices had their library closed, while other parts of EPA were unaffected.

> "The sample is not designed so that results can be extrapolated to a total population (a condition which is not made clear throughout report)."[24]

As is clearly stated in the report, "it is difficult to extrapolate these raw numbers to a percentage of the EPA's total scientific workforce."[25] Nowhere in the report do we extrapolate our findings to the total population. In presenting the survey results, we consistently emphasize raw numbers of respondents and include percentages primarily for comparison.

The one place in the report where percentages of respondents are emphasized is the comparison of responses to question 39 across the various offices, regions and divisions of the EPA. The CRS report states that "it is not clear whether the denominator of the percentages is all of the respondents in the study or all of the respondents in each of the divisions."[26] This question is answered at the start of Appendix B, where we provide the complete organizational breakdown for question 39 and explain "The percentages in each table are based on the total number of scientists from each office or location who answered each question."[27] While this information is available in the report, we could have made it clearer in the report text itself and we regret any confusion that might have caused our readers.

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[23] CRS, p. 8.
[24] CRS, p. 7.
[25] UCS, p. 21.
[26] CRS, p. 7.
[27] UCS, p. 75.